CHEMPARTNER
DEDICATED TO LIFESCIENCE

DMPK BIOANALYSIS

CAPABILITIES

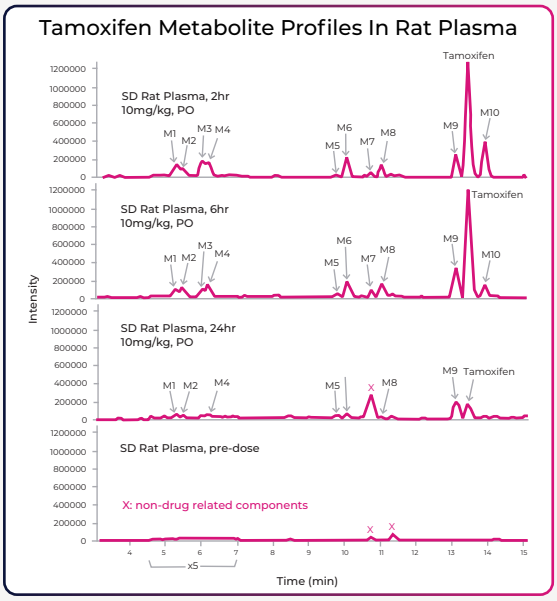
SMALL MOLECULES

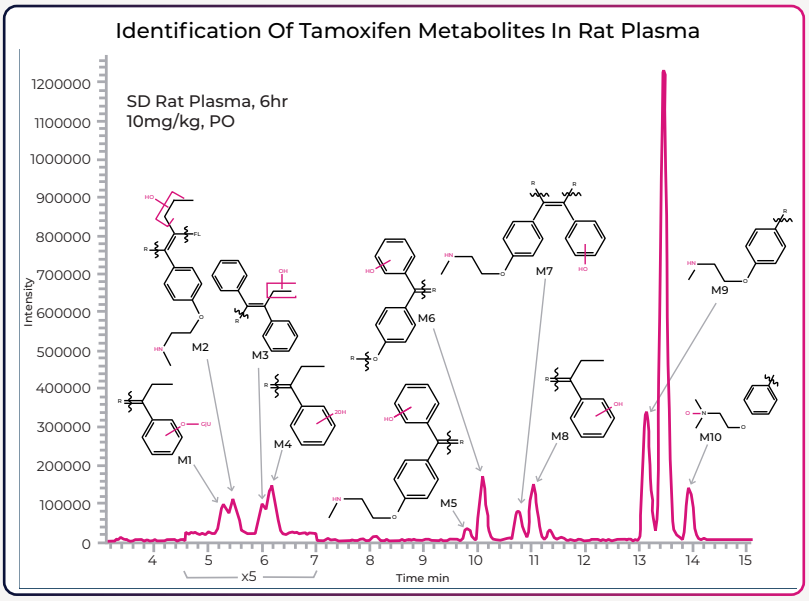
- Mass spectrometry-based analysis
- Parent and metabolites from PK, PK/PD, in vitro ADME, metabolite identification
- Matrices: biological fluids and tissues

LARGE MOLECULES

- ELISA and MSD and mass spectrometry-based analysis
  - PK, PK/PD, biomarker test and immunogenicity test
  - Bioassay

METABOLOMICS AND BIOMARKER ANALYSIS CASE STUDIES





BIOMARKER ANALYSIS

- A set of cell pellets produced with known numbers of cells
- Extracts made and analyzed by LCMS/MS
- Resulting acetyl CoA in extract plotted against numbers 1of the cells loaded
- LC-MS/MS signal responses correlated with cell numbers
- Optimized cell numbers, washing factor evaluated and cell handling time optimized

REGULATED BIOANALYSIS

ASSAY METHOD FOR DOXORUBICIN QUANTIFICATION

- Objective
  - Due to in vivo PK difference, separation of free and encapsulated drug in plasma is needed
- Challenge
  - Liposome is fragile
  - Heat exposure, non-isotonic condition and thawing can produce premature bursting of the lipsome
  - Sample preparation
- SPE Procedures
  - SPE plate selection
  - SPE procedure optimization
- LC-MS/MS Conditions
  - Column: Waters Xbridge C18 (2.1X50 mm, 3.5 um)
  - Mobile phase: Water: Acetonitrile: Formic Acid (10:90:0.2, v/v/v/)
  - API 6500, TIS, positive

QUALIFICATION ELEMENT			RESULTS	CRITERIA
Accuracy	Calibration Curve (n=6)	20.0~2000pg/ml	-2.8%~3.2%	Accuracy within ±15.0%, except LLOQ within ±20.0%
Accuracy	Intra-assay (n=6)	LLOQ QC	5.2%	Within±15.0%, except at the LLOQ where it should be within ±20.0%
		Low QC	1.8%	
		Medium QC	2.5%	
		High QC	-2.5%	
	Inter-assay (n=18)	LLOQ QC	2.7%	Within±15.0%, except at the LLOQ where it should be within ±20.0%
		Low QC	2.0%	
		Medium QC	2.7%	
		High QC	1.1%	
Precision	Intra-assay (n=6)	LLOQ QC	8.4%	≤15.0% except at the LLOQ where it should not exceed 20.0%
		Low QC	3.4%	
		Medium QC	2.8%	
		High QC	3.0%	
	Inter-assay (n=18)	LLOQ QC	8.1%	≤15.0% except at the LLOQ where it should not exceed 20.0%
		Low QC	3.2%	
		Medium QC	2.8%	
		High QC	3.9%	
Selectivity	Plasma (n=6)		No interference	<20.0%of the mean response of the accepted LLOQ
Dilution Integrity	Dilution Factor: 20	Accuracy	5.8%	Within±15.0%
		Precision	2.4%	≤15.0%
Robustness	Plasma Stability	RT (8 hr)	-6.5%~1.8%	Accuracy within ±15.0% for 2/3 samples
		LT (-70°C, 30 days)	-6.4%~6.1%	
		FT (4 cycles)	-7.5%~-1.1%	
	Blood Stability	48 min	-0.8%~-0.3%	Ratio difference between Tn and T0 within ±15.0%
Extraction Recovery	Recovery	Low QC	86.3%	%CV≤20.0%
		Medium QC	83.3%	
		High QC	88.7%	
	Precision (CV%)		3.1%~5.6%	
Matrix Effect	IS-normalized MF	Low QC	3.6%	IS-normalized MF <15.0%
		High QC	2.2%	

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