



GCC Center for Comprehensive PK/PD & Formulation (CCPF)



- Dong Liang, Ph.D. (TSU)
- Huan Xie, Ph.D. (TSU)
- Diana S-L Chow, Ph.D. FNAI (UH)
- Omonike Olaleye, Ph.D., MPH (TSU)
- Suzanne Tomlinson, Ph.D. (GCC)

Huan Xie, PhD, Professor of Pharmaceutics, TSU



Education:

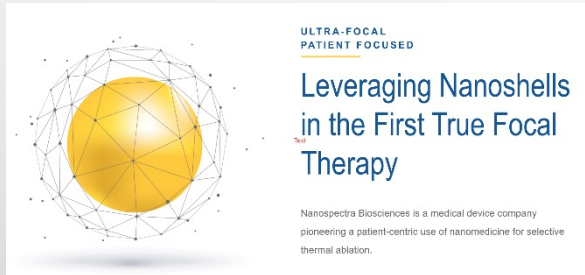
- B.S. in Chemistry, Fudan University, Shanghai, 1999
- Ph.D. in Chemistry, North Carolina State University, Raleigh, 2004

Employment:

- Nanospectra Biosciences, Houston, 2004-2008
- Texas Southern University, Houston, 2008-

Positions:

- Co-Director of CPRIT-CCPF Core: 2018-present
- PI of NIH-RCMI Center for Biomedical and Minority Health (CBMHR): 2020-
- Program Director of Graduate Program of Pharmaceutical Sciences (GPPS): 2020-
- Area of interest: drug characterization, formulation, drug delivery, pharmacokinetics and pharmacodynamics, nanotechnology



FORMULATION DEVELOPMENT

PK/PD CHARACTERIZATION

Pre- and Formulation

1. Drug Characterization

- Solubility
- pKa
- Log P
- Stability

2. Basic Formulation:

- Cosolvent
- Cyclodextrin
- Dispersed systems

3. Advanced Drug Delivery:

- Micro/nanoemulsions
- Liposomes
- Nanoparticles



CENTER FOR COMPREHENSIVE
PK|PD + FORMULATION

PK/PD CHARACTERIZATION

Pre-clinical PK/PD Evaluations

4. Bioanalysis

- Method development and validation to quantitate concentrations of drug or metabolite in biological matrix
- Identification of unknown metabolites using accurate mass

5. In Vitro Metabolism

- Drug metabolism characterization using tissue microsomes, S9 fraction, and Recombinant enzymes
- Metabolite profiling & identification

6. In Vitro Biopharm Characterization

- Membrane permeability and transporter identification
- Bindings to plasma proteins, albumin or α -glycoprotein

7. In Vivo PK

- PK studies in rats and mice after IV, oral, IP and SC drug administration
- Dose linearity PK studies
- Bioavailability studies
- PK studies on tissue distribution

8. In Vitro/In Vivo PD

- Cell proliferation assay
- Apoptosis assay
- DNA damage assay
- Migration/invasion assays
- Xenograft assay
- Biomarker assays on tumors from xenograft models
- Genetic mouse models for PD assays

9. PK/PD Modeling and Simulation

- Consultation on experimental design
- PK modeling development and simulation
- PD modeling and determination of parameters
- PK/PD modeling

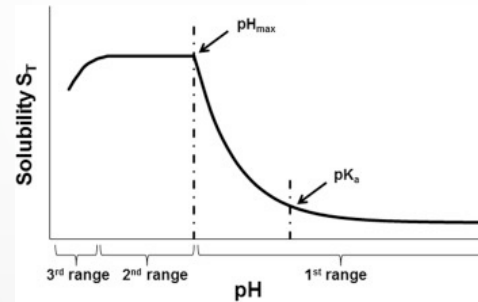


PRE-FORMULATION AND FORMULATION

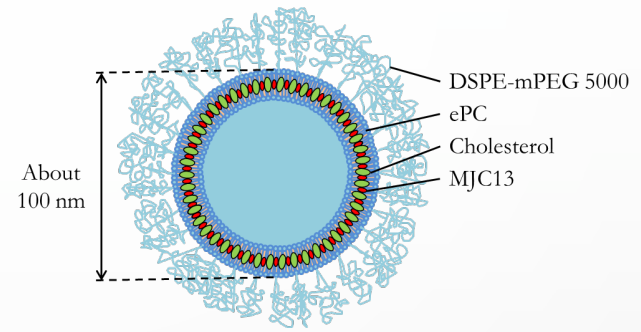
Pre-formulation characterization:
pKa, pH-solubility profiles, logP



Pion SiriusT3

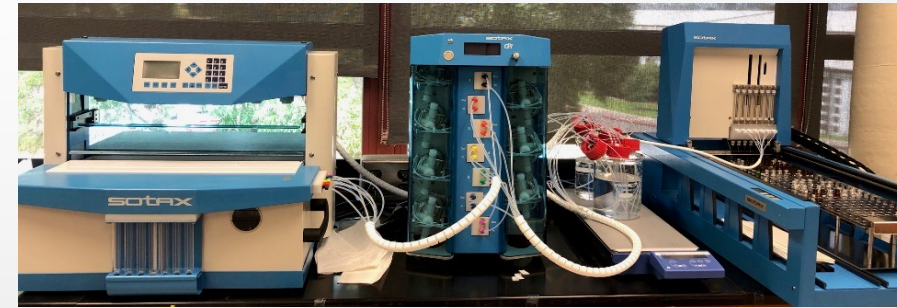
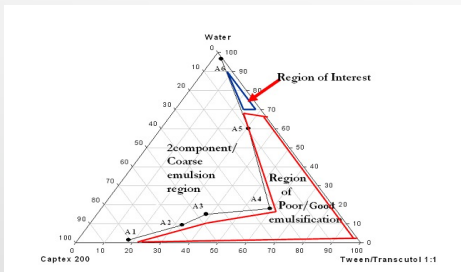
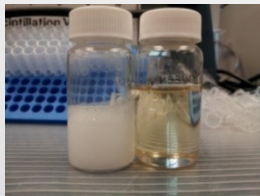


Nano drug delivery systems (NDDS)



Label	Material			Encapsulation efficiency (%)
	MJC13 (mg)	Egg PC (mg)	Cholesterol (mg)	
A	10	200	0	43.4
B	10	200	10	62.8
C	10	200	20	75.2
D*	10	200	25	78.3
E	10	200	30	74.8
F	10	200	40	67.1

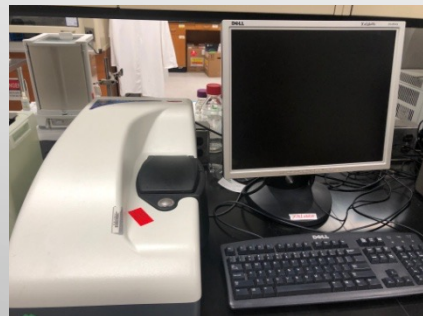
Formulation development



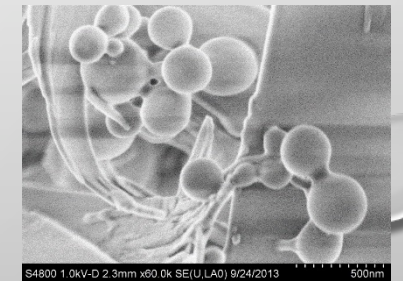
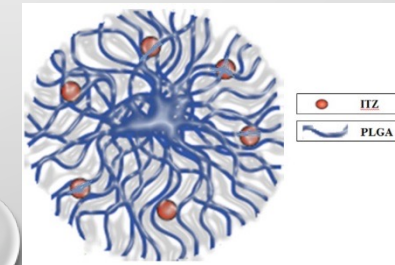
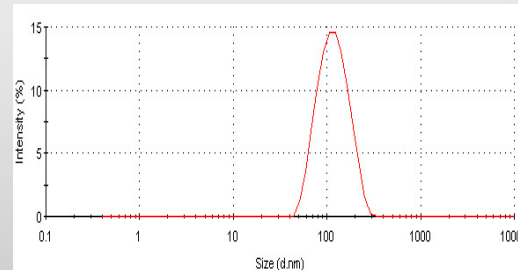
SOTAX CE 7smart USP Apparatus 4



Microfluidics



Zetasizer



Bian et al, *Int J Nanomedicine*, 8:4521-31, 2013

Dong Liang, PhD, Professor of Pharmaceutics, TSU



B.S. in Pharmacy in 1985
M.S. in Pharmaceutics 1988



1st Job in a Pharmaceutical Company



Ph.D. in Pharmaceutics in 1995

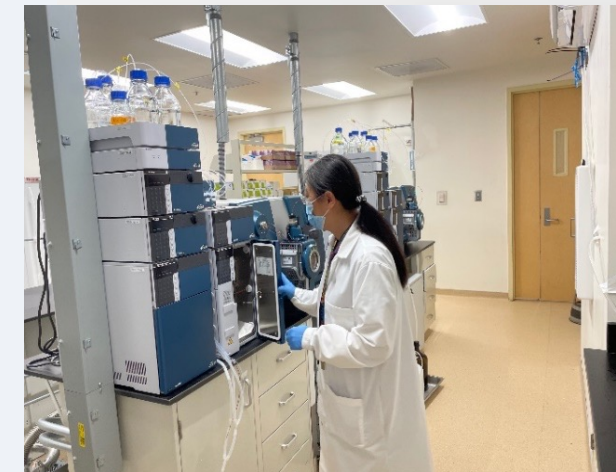
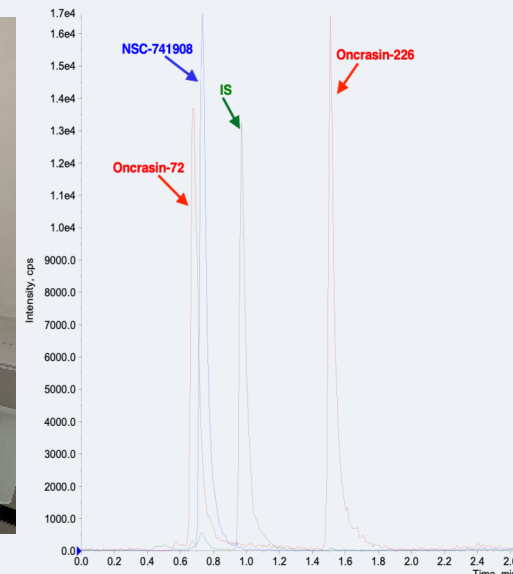
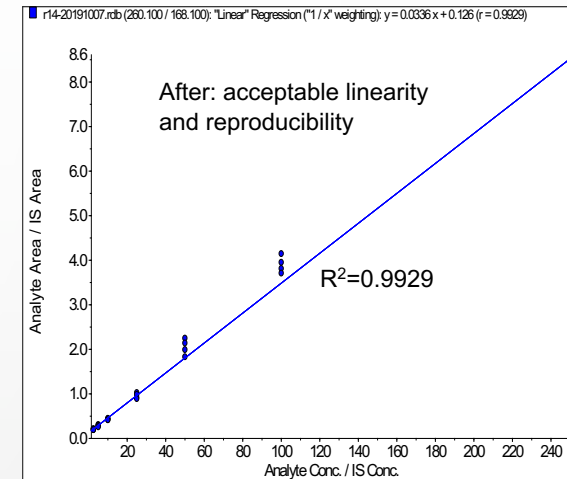
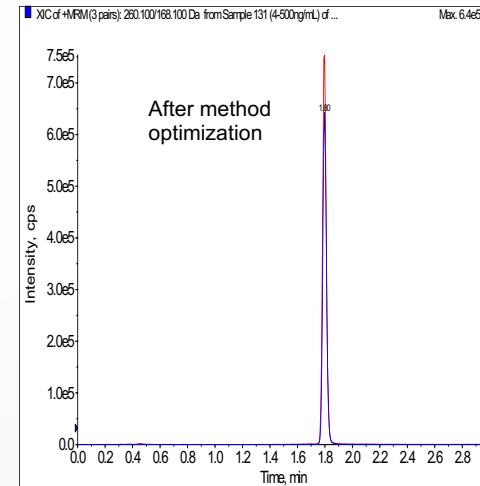
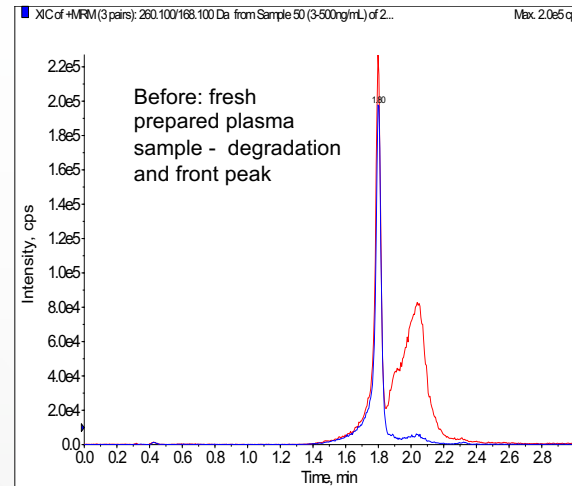
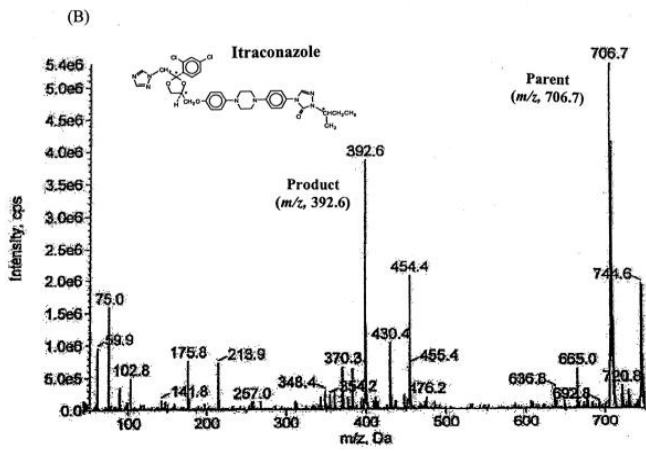
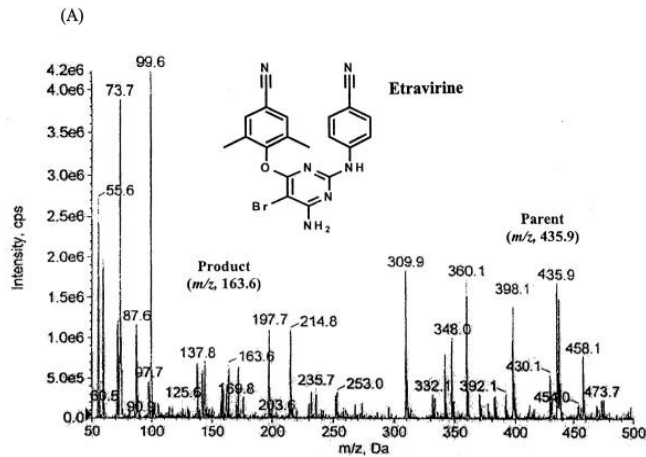


Joined TSU COPHS in 1998

- DMPK Department – Research Scientist
- Phase 1 PK studies: protocol design, site qualification, CRF, dosing & sampling, bioanalytical, PK analysis
- 42 generic ANDAs & 3 NDAs

- Program Director of RCMI 2008-present
- Co-Director of CCPF Core 2018-present
- Area of interest: bioanalysis, biopharmaceutics, & pharmacokinetics

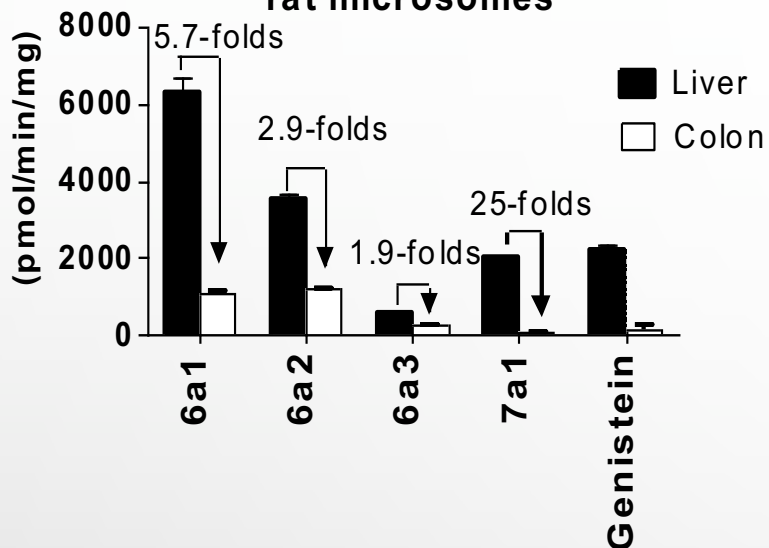
BIOANALYSIS: LC-MS/MS QUANTITATION OF DRUGS & METABOLITES IN BIOLOGICAL SAMPLES



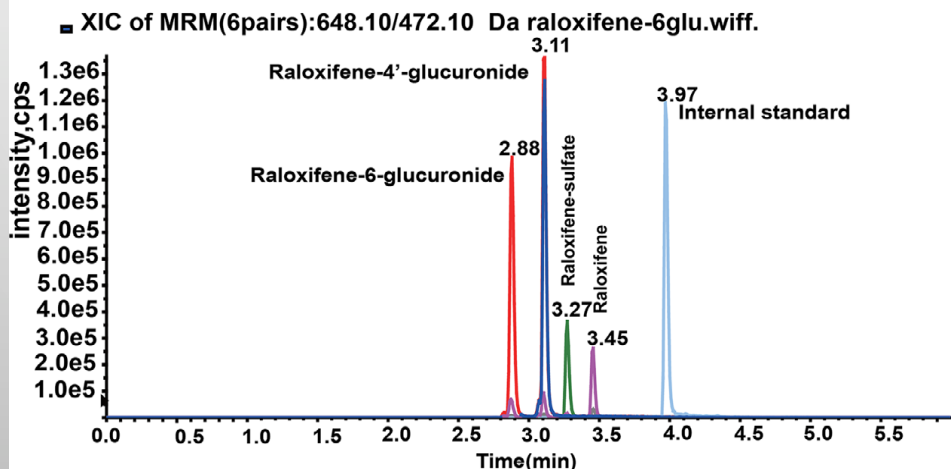
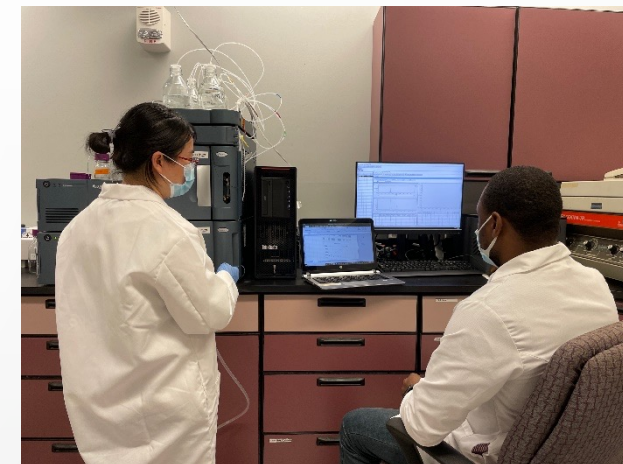
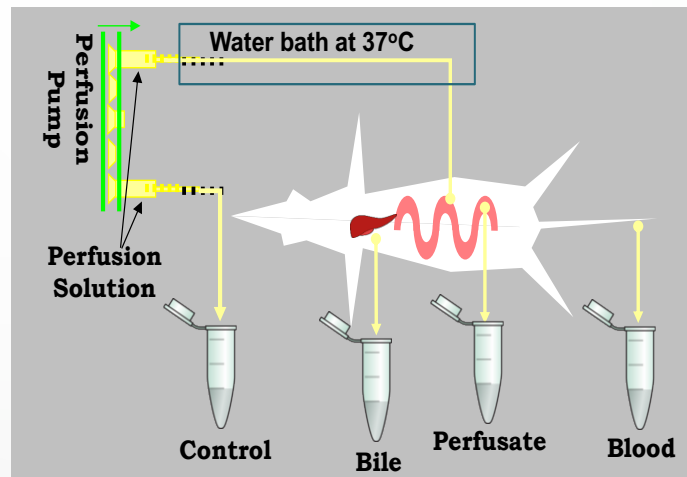
White L, et al. *J Chromatogr B*, 1033-4:106-11, 2016

IN VITRO DRUG METABOLISM & IN SITU PERMEABILITY

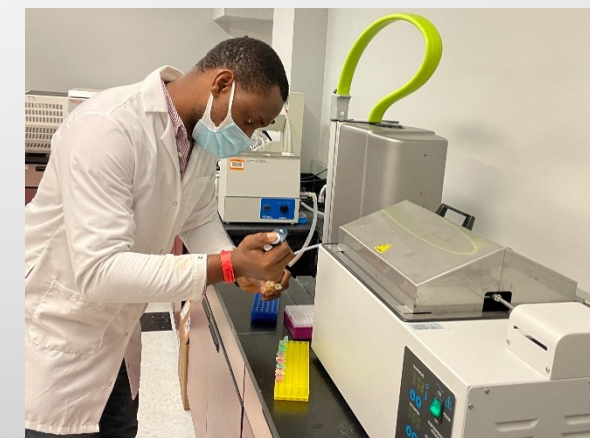
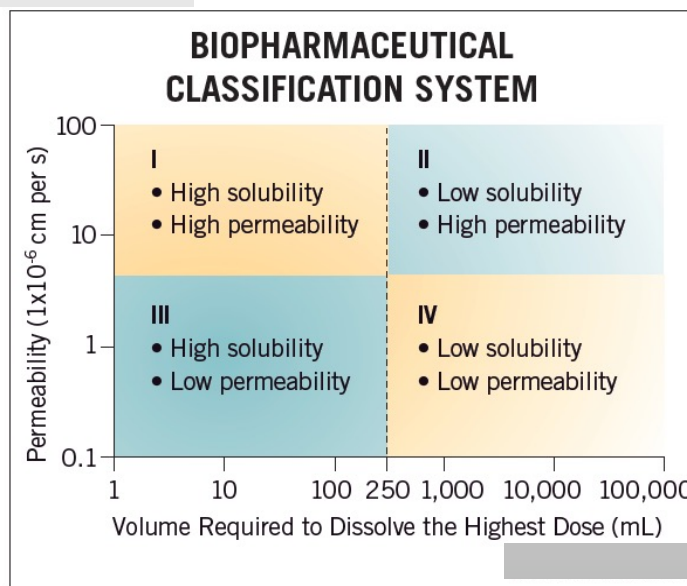
Glucuronidation rates with rat microsomes



Intestinal absorption and biliary secretion of a celecoxib derivative

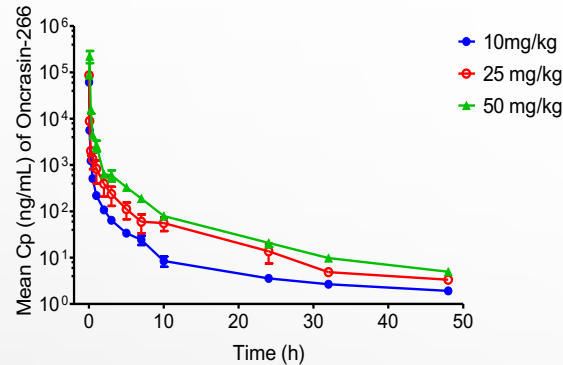


Du T, et al. *J Sep Sci*, 43:4414-23, 2020



PHARMACOKINETIC (PK) & BIODISTRIBUTION STUDIES

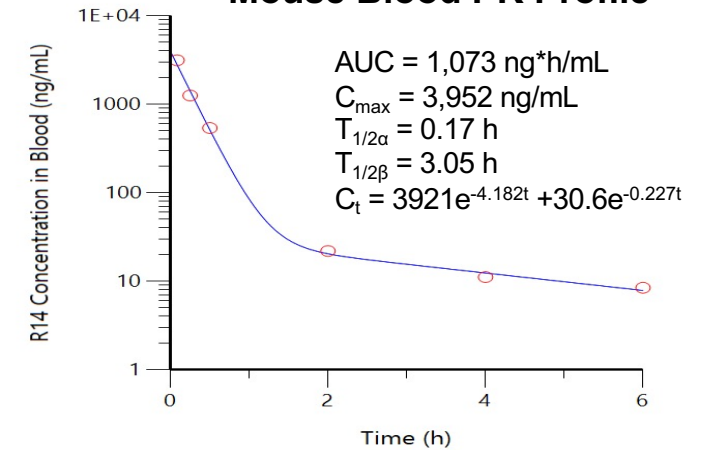
Jugular vein cannulated, rat PK studies in metabolism cage



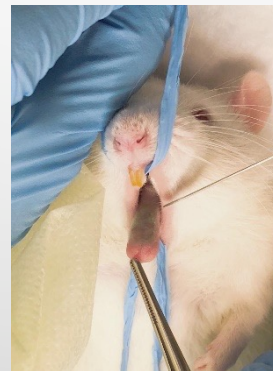
Mouse PK studies via tail vein



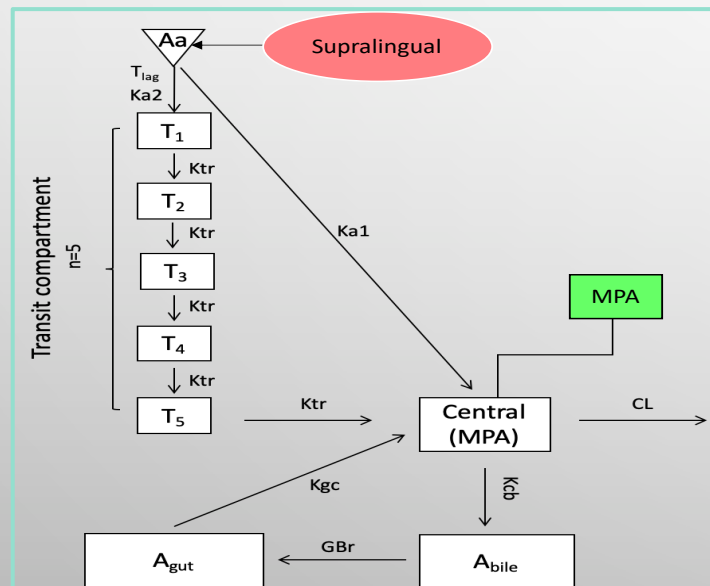
Mouse Blood PK Profile



Patch tongue distribution study



Gao et al, *Pharmaceutics*. 2021 Apr; 13(4): 574.



		IV (n=5)	Oral (n=3)	Supralingual (n=3)
Parameter	Unit	Mean	Mean	Mean
Dose	mg/kg	0.5	0.5	0.5
T _{au}	hr	1.5 ± 0.5	4.5 ± 4.7	31.5 ± 11.6
Half-life	hr	10.5 ± 1.2	7.4 ± 2.1	11.5 ± 3.0
CL	mL/(kg*hr)	116.6 ± 92.2	99.9 ± 61.7	16.4 ± 23.2
CL ₂	mL/(kg*hr)	224.0 ± 65.5	194.5 ± 119.9	NA
K _{cb}	1/hr	1.4 ± 1.0	10.3 ± 0.8	0.1 ± 0.1
K _{gc}	1/hr	2.0 ± 2.0	7.8 ± 8.5	32.4 ± 52.3
V	mL/kg	110.3 ± 10.8	21.0 ± 7.3	232.1 ± 7.1
V ₂	mL/kg	1739.2 ± 508.0	2242.0 ± 1458.4	NA
K _{a1}	1/hr	NA	1.0 ± 0.3	21.6 ± 14.6
K _{a2}	1/hr	NA	1.5 ± 0.4	37.3 ± 22.7
K _{tr}	1/hr	NA	1.3 ± 0.1	0.20 ± 0.0
AUC ₀₋₄₈	ng*hr/mL	2172.8 ± 355.3	1573.1 ± 217.6	132.1 ± 16.8
F _{abs}	%	NA	72.4 ± 10.1	7.6 ± 1.0 *

Diana S-L Chow, PhD, FNAI, Professor of Pharmaceutics, UHCOP



(1981-2017)

(2018-)

- Director, Institute for Drug Education and Research (IDER)
- PD/PI of NCI P20 – Cancer Drug Discovery/Development and Education, partnering with BCM – DLDC, 2018-present
- PI of PK/PD Core of CPRIT- CCPF Program, 2018-present
- Areas of interest:

Repurposing Medications,

Formulation Optimization

IND-enabling Preclinical PK, PD
Research

Translational and Clinical PK/PD/PG



IN VITRO/ IN VIVO PHARMACODYNAMICS (PD)

In Vitro PD

- Cell proliferation assay
- Apoptosis assay
- DNA damage assay
- Migration/invasion assays

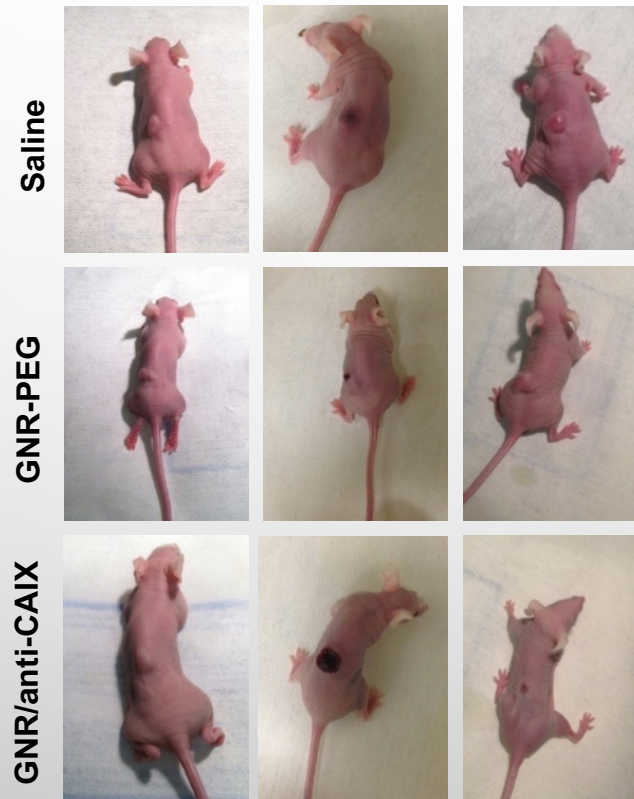


In Vivo PD

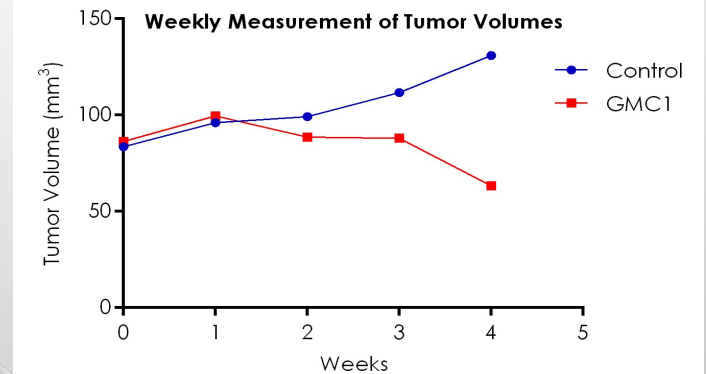
- Xenograft assay
- Biomarker assays on tumors from xenograft models
- Genetic mouse models for PD assays



Treatment Day (Day 0) Day 1 After Treatment Day 16 After Treatment



Castrated Male Athymic Nude Mice Injected with LNCaP-ID4 Cells



PK/PD MODELING AND SIMULATION

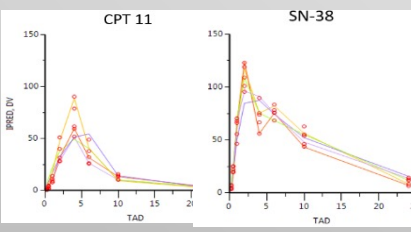
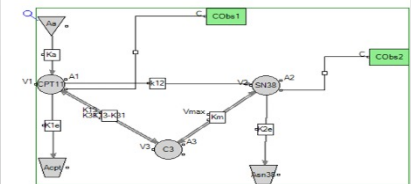
PK Modeling

Software

- Phoenix Modeling Individual and Pop PK
- GastroPlus PK Analysis and PBPK
- WinNonlin PK Analysis

Project Examples:

- Intranasal Scopolamine PK Analysis
- Irinotecan (CPT-11) PK Analysis
- Co-modeling of Parent Comp'd and Metabolite:



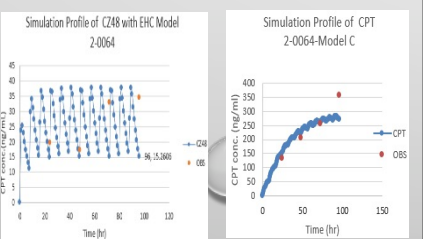
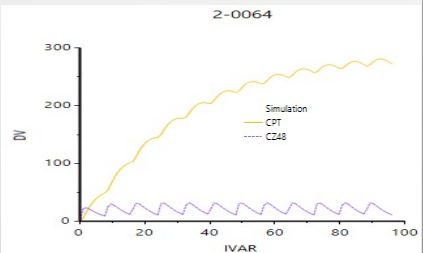
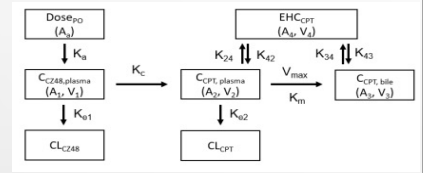
PK Modeling and Simulation

Software

- Phoenix Modeling
- GastroPlus

Project Example:

- Clinical Trail of CZ48 and CPT
- EHC and Simulation:



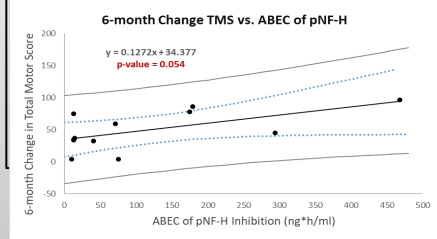
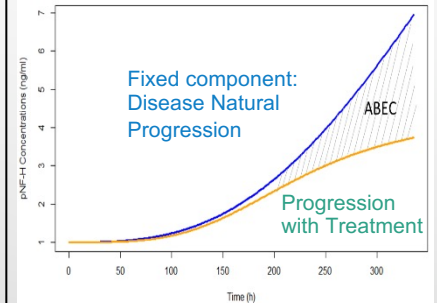
PD Modeling

Software

- Phoenix Modeling
- GastroPlus
- WinNonlin
- Design Expert Factors Correlation

Project Example:

- Riluzole PD Study in Acute Spinal Cord Injured Patients - Progressive Disease Model



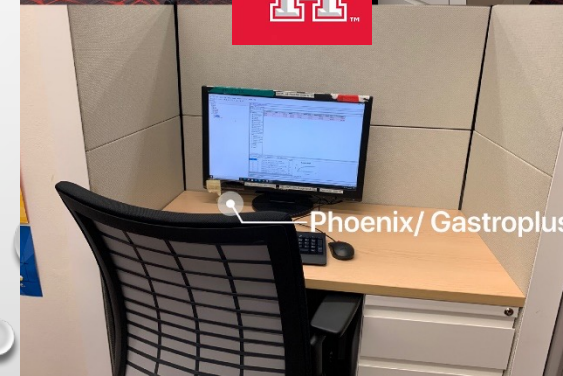
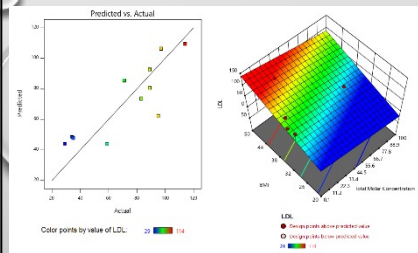
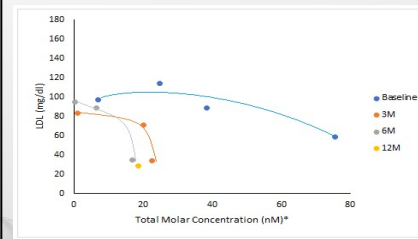
PK/PD Modeling

Software

- Phoenix Modeling
- GastroPlus
- WinNonlin
- Symcyp PKPD and Simulation

Project Example:

- Clinical Statin PK/PD Analysis Post Gastro Bypass Surgery
- Atorvastatin PK/PD Modeling:



Allometric (Interspecies) Scaling Applications

- IMPROVE AND EXPEDITE DRUG SELECTION AND DEVELOPMENT-
SELECTION OF FIH
- WIDELY USED TO EXTRAPOLATE PK PARAMETERS FROM **ANIMAL TO HUMAN**, BASED ON THE SIMILARITY OF ANATOMICAL, PHYSIOLOGICAL AND BIOCHEMICAL VARIABLES IN MAMMALS
- PREDICT TOXICOLOGICAL ENDPOINTS IN HUMANS
- SELECT EQUIVALENT DOSAGE REGIMENS IN HUMANS

LESS D, LONGER τ

Allometric (Interspecies) Scaling Applications (Cont'd)

- CLINICAL TRIAL SIMULATION AND OPTIMIZATION OF PHASE I DOSING STRATEGIES FOR **PEDIATRIC** PATIENTS, BASED ON PK IN ADULTS, AND IN NEONATAL AND JUVENILE ANIMAL MODELS.
- CLINICAL TRIAL SIMULATION AND OPTIMIZATION OF PHASE I DOSING STRATEGIES FOR **OBESE** PATIENTS, BASED ON PK IN LEAN PATIENTS

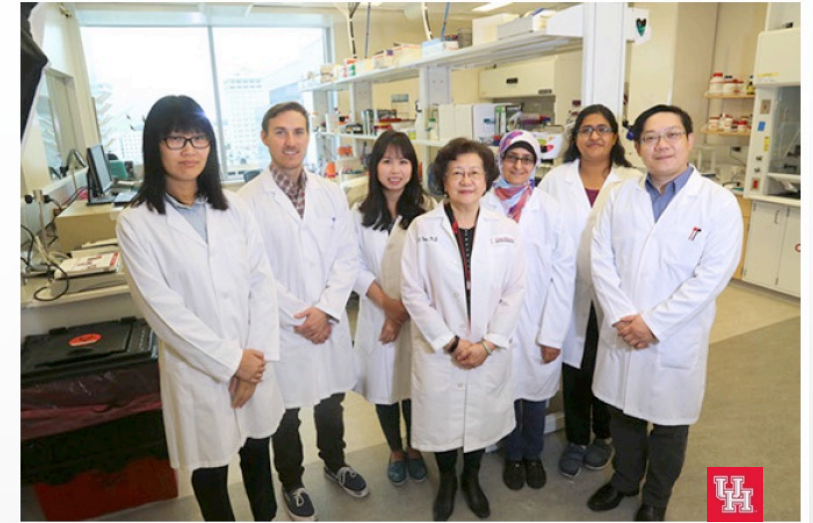
CCPF FACILITY AND GROUP



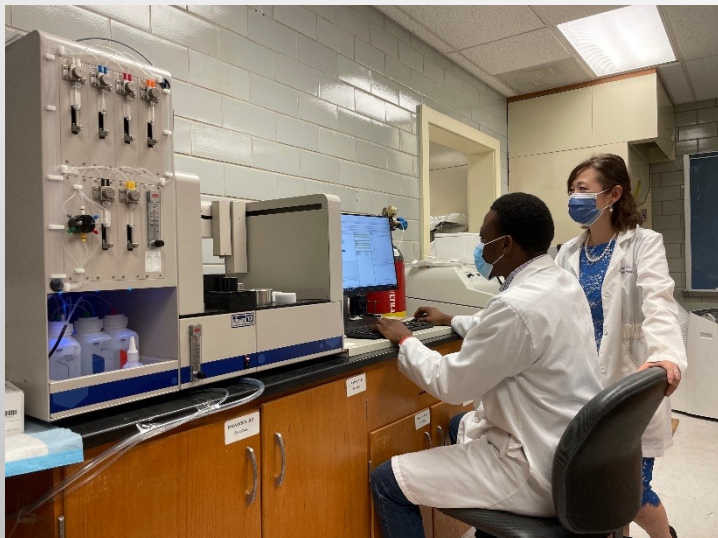
TSU CCPF Office Suite



Conference Room



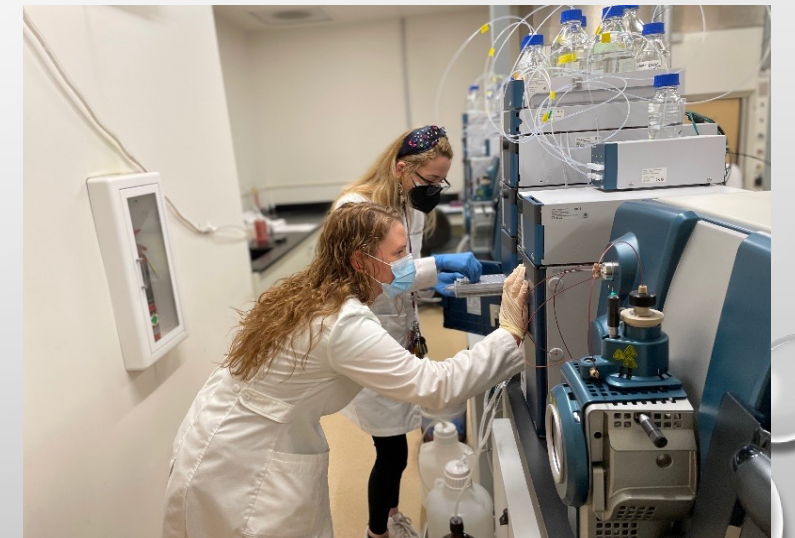
UH PK/PD Modeling Lab



Formulation Lab



Biopharmaceutics Lab



LC-MS/MS Instrument Lab

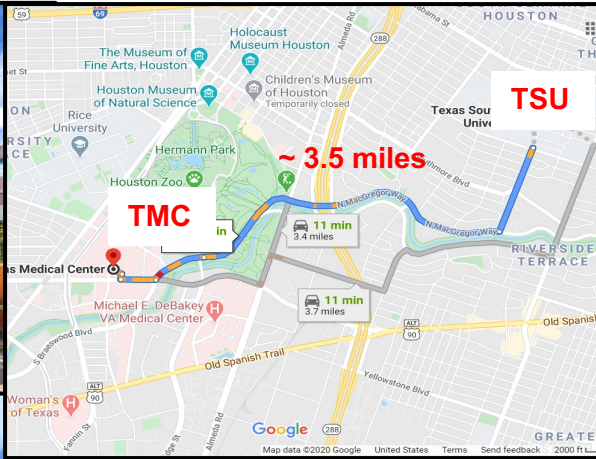
WELCOME TO TSU

CBMHR
CENTER FOR BIOMEDICAL & MINORITY HEALTH RESEARCH

NIH National Institute on Minority Health and Health Disparities

\$8.63M

**Bridge Health Disparities
Community Outreach & Engagement**



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<https://www.gcc-ccpf.com/>

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Welcome to CCPF

Gulf Coast Consortia (GCC) Center for Comprehensive PK/PD & Formulation (CCPF) provides pre-clinical drug development services from formulation development to PK/PD characterization.



SERVICES

Our services include a wide variety of in vitro, in situ and vivo studies in nine specific areas.

Drug Characterization

Determine the physicochemical properties of drug candidates.

[Learn more](#)

Basic Formulation

Prepare suitable formulation with reasonable solubility and bioavailability for initial animal testing

[Learn more](#)

Advanced Drug Delivery Systems

Further improve the PK profiles and bioavailabilities of promising drug candidates with nanoformulation.

[Learn more](#)

Bioanalysis

Develop and validate specific, sensitive and reproducible LC-MS/MS methods to quantitate drugs or metabolites in biological matrix.

[Learn more](#)

In Vitro Metabolism

Determine drug metabolism using enzyme-mediated reactions.

[Learn more](#)

In Vitro Biopharm Characterization

Understand membrane permeability to predict drug absorption.

[Learn more](#)