OCT 25-28 2026

aaps PharmSci 360

Advancing NAMs with Quantitative Systems Toxicology and Microphysiological Systems

October 27, 2026

Jeff Woodhead, Ph.D.

Session Description and Objectives

- Quantitative systems toxicology (QST) is a proven method for translating *in vitro* inputs to toxicity predictions
- Biologics and other non-small-molecule treatment modalities present different translational challenges
- QST can help translate novel NAM-derived data into toxicity predictions

- Understand how QST makes predictions from *in vitro* data inputs
- Understand the unique QST challenges presented by large molecules
- Understand how large molecule NAM-based *in vitro* data can be used as QST inputs

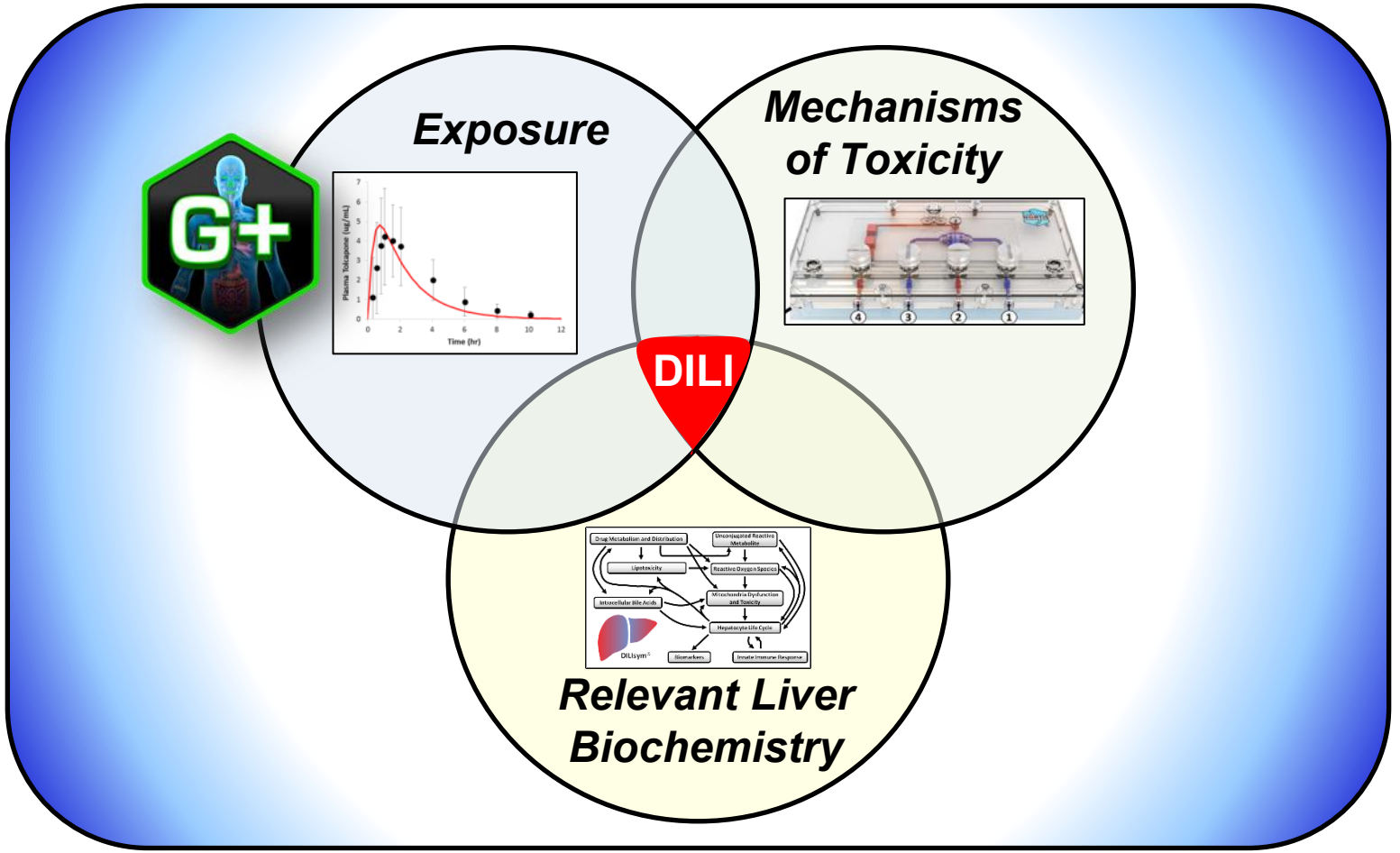
Biography and Contact Information

- Jeff Woodhead, Ph.D., Senior Principal Scientist, Simulations Plus
- 15 years QSP/QST experience
- Director, DILI-sim Initiative
  - Precompetitive consortium responsible for directing the development of DILIsym, a QST model of liver injury widely regarded as the industry standard for liver QST modeling
- Leader of the QSP R&D group at Simulations Plus
- Email: jeff.woodhead@simulations-plus.com

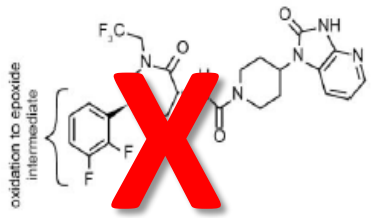
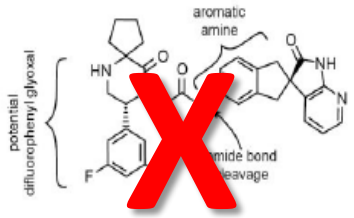
Agenda

- Intro to QST and the DILIsym workflow
- Translation to biologics – BIOLOGXsym
- Novel biologic-induced toxicity mechanisms
- Next steps: siRNA drugs and other liver-on-a-chip systems

Quantitative Systems Toxicology Integrates Biochemistry Knowledge and Experimental Results for High-Quality Predictions



Example DILIsym Workflow: Calcitonin Gene-related Peptide (CGRP) Receptor Antagonists for Treatment of Migraines

Parameter	Telcagepant[a]	MK-3207[b]
Structure[d]		
Potency IC_{50}[e]	2.2 nM	0.12 nM
Pivotal conventional nonclinical toxicology study liver findings	3M rat: <3 × ALT/AST with no liver histopathology at 15× exposure margin 6M rat: no liver safety signal at 7x margin 9M NHP: no liver safety signal at 7× margin 6M mouse: <2 × ALT/AST with no liver histopathology at 14× margin	6M rat: no liver safety signal at 25× exposure margin 9M NHP: no liver safety signal at 4× margin 6M mouse: no liver safety signal at 12× margin 1M dog: slight periportal vacuolation with <4 × ALT/AST associated with excessive body weight loss at 17x margin

Next-in-class Compounds

- Ubrogepant ?
- Rimegepant ?
- Atogepant ?
- Zavegepant ?

Data Used for CGRP Antagonist Compound Projects

PBPK Modeling

- **Compound Properties**
  - Tissue partition coefficients
- **Tissue penetration studies**
  - *Liver to blood ratio*
- **Pharmacokinetic data**
  - *Absorption, extra-hepatic clearance, metabolites*
- ***in vitro* data**
  - *Metabolite synthesis, active uptake*

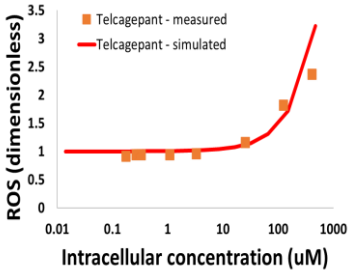
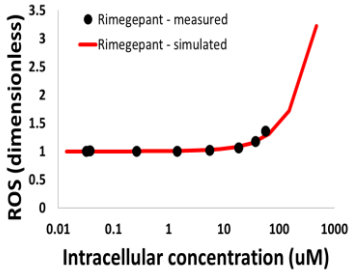
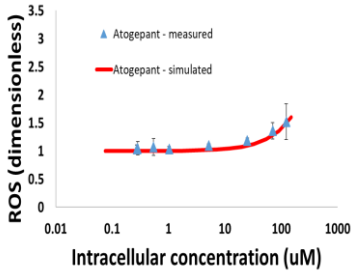
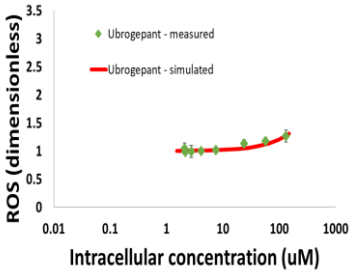
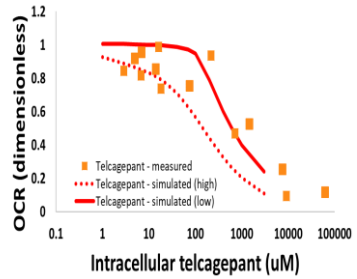
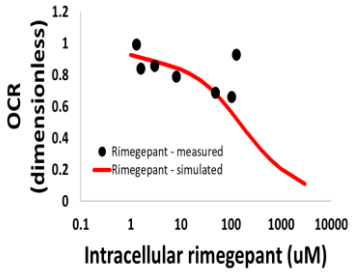
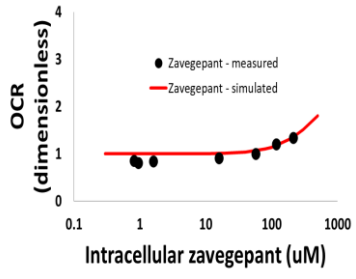
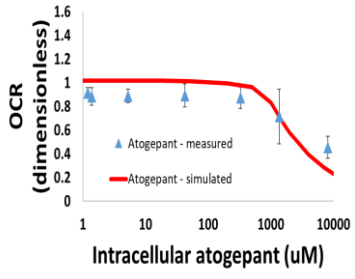
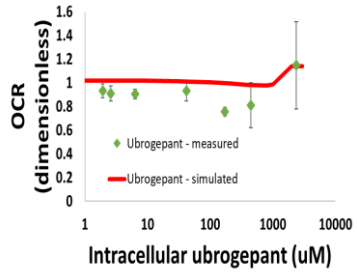
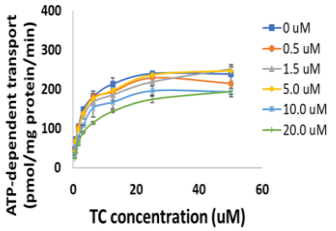
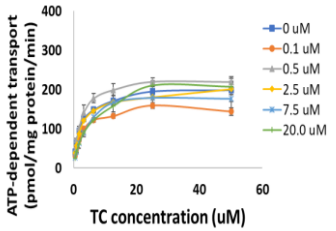
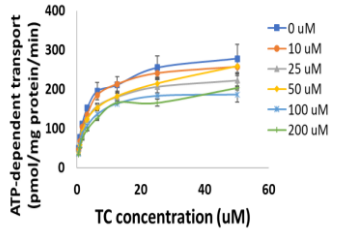
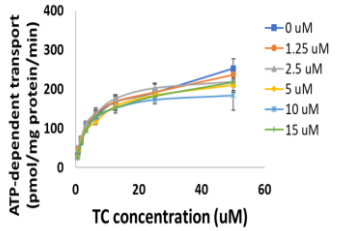
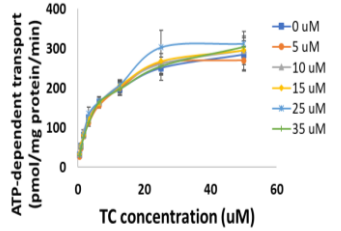
- **Telcagepant**: published clinical PK data
- **Rimegepant**: internal clinical PK data available
- **Zavegepant**: ADMET Predictor informed by animal data and intra-nasal dosing route
- **Atogepant**: pure IVIVE using ADMET Predictor
- **Ubrogepant**: pure IVIVE using ADMET Predictor

Data Collected for Quantitative DILI Mechanism Info

- **Oxidative stress** *(high content imaging)*
  - *Direct and reactive metabolite-mediated*
- **Mitochondrial toxicity** *(XF Analyzer)*
  - *ETC inhibition*
  - *Uncoupling*
- **Bile acid / phospholipid transporter inhibition**
  - *BSEP, MRP3 and 4, NTCP, MDR3*
- **Bilirubin transport/metabolism**
  - *OATP1B1, OATP1B3, UGT1A1, MRP2, MRP3*

- Full in vitro data set collected for all five compounds

In Vitro Mechanistic Toxicity Signals Observed for Telcagepant, Rimegepant, Zavegepant, Atogepant, and Ubrogepant

Mechanism	In Vitro Assay	Telcagepant	Rimegepant	Zavegepant	Atogepant	Ubrogepant
Oxidative Stress	HepG2 cells; High content imaging			***No ROS Signal***		
Mito-chondrial Dysfunction	HepG2 cells; Seahorse XF analyzer					
Bile Acid Transporter Inhibition	Membrane vesicles & transfected cells; Transport of taurocholate					

Woodhead et al., Tox Sci (2022)

CGRP Antagonist Compound Simulation Results

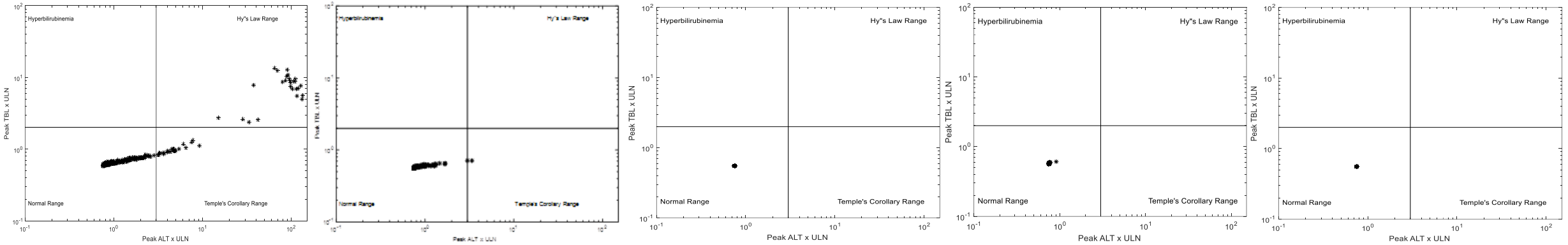
Telcagepant; 140 mg BID, 12 weeks, high ETCi

Rimegepant; 75 mg QD, alternate day dosing, 14 total doses over 28 days

Zavegepant; 20 mg IN or 750 mg PO or 7.5 mg IV, 25 straight days

Atogepant; 60 mg BID, 12 weeks

Ubrogepant; 100 mg QD, 25 straight days



- Telcagepant toxicity correctly predicted by DILIsym
- Rimegepant predicted to be safe at clinical doses, with mild ALT elevations occurring only in extreme dosing conditions
- Zavegepant, atogepant, and ubrogepant all predicted to be safe with substantial safety margins

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Large Molecule Therapeutics Comprise a Growing Segment of the Approved Drug Pipeline

Historical record for new molecular entities and biologics approved by the FDA

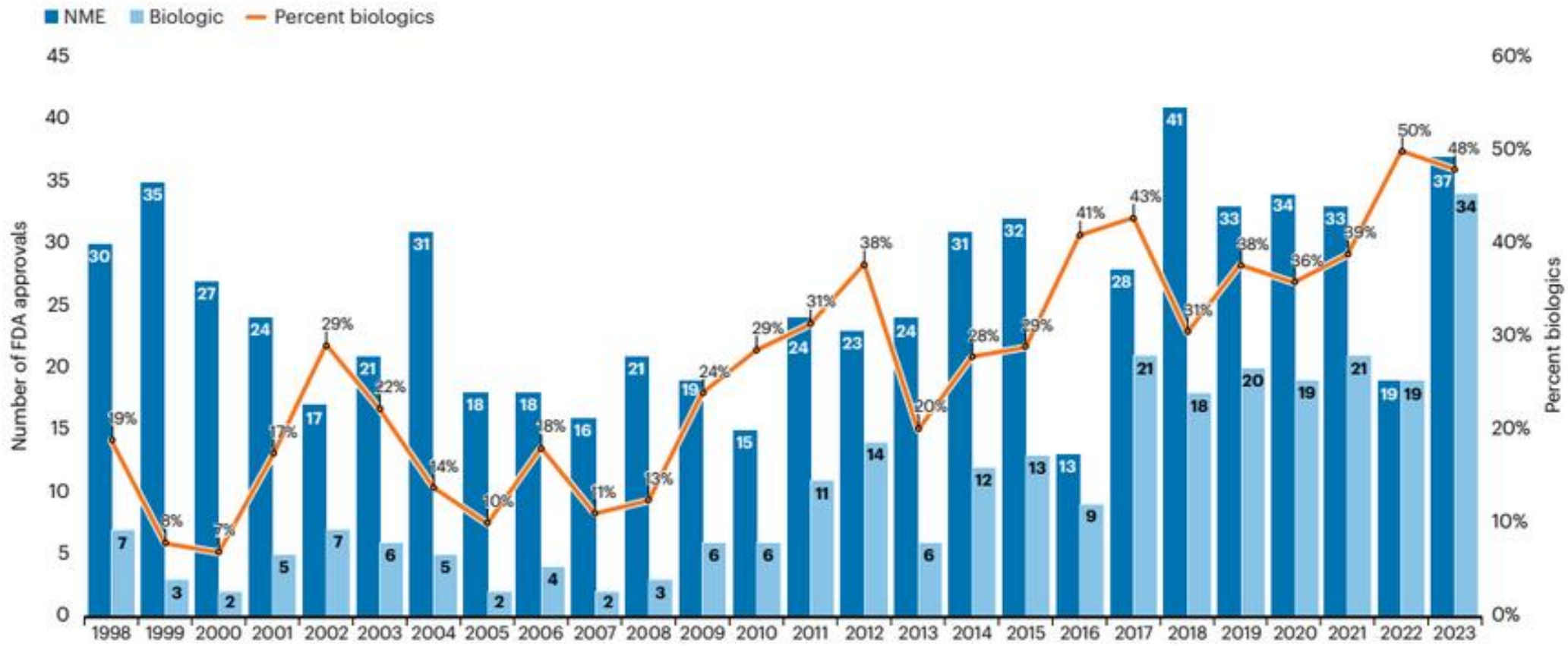
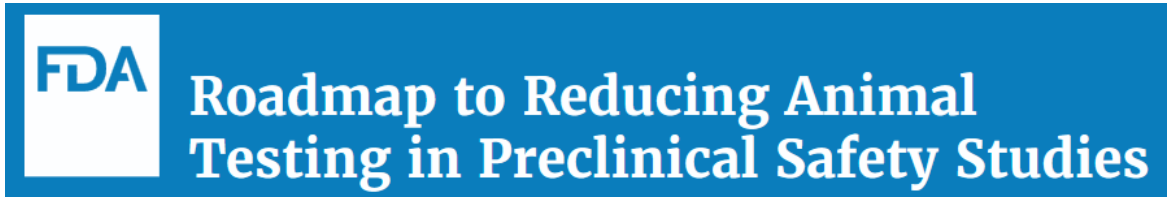


Fig. 1 | FDA new drug approvals (CDER and CBER). The US regulator approved record numbers of new drugs in 2023.

Senior 2024, PMID 38409589

Monoclonal Antibodies Show Liver Safety Issues and Were Targeted for NAM Replacement of Preclinical Safety Studies

- In April 2025, the FDA announced a roadmap to reduce animal testing in preclinical safety studies, starting with monoclonal antibodies (mAbs)
  - Multiple mAbs have been associated with liver injury, including those targeting cytokines, B cells, immune checkpoint molecules
- In March 2026, the FDA released a draft guidance on the use of new approach methodologies in drug development, describing weight-of-evidence approaches that include in vitro assays, computational methodologies, and other models to generate evidence for safety endpoints

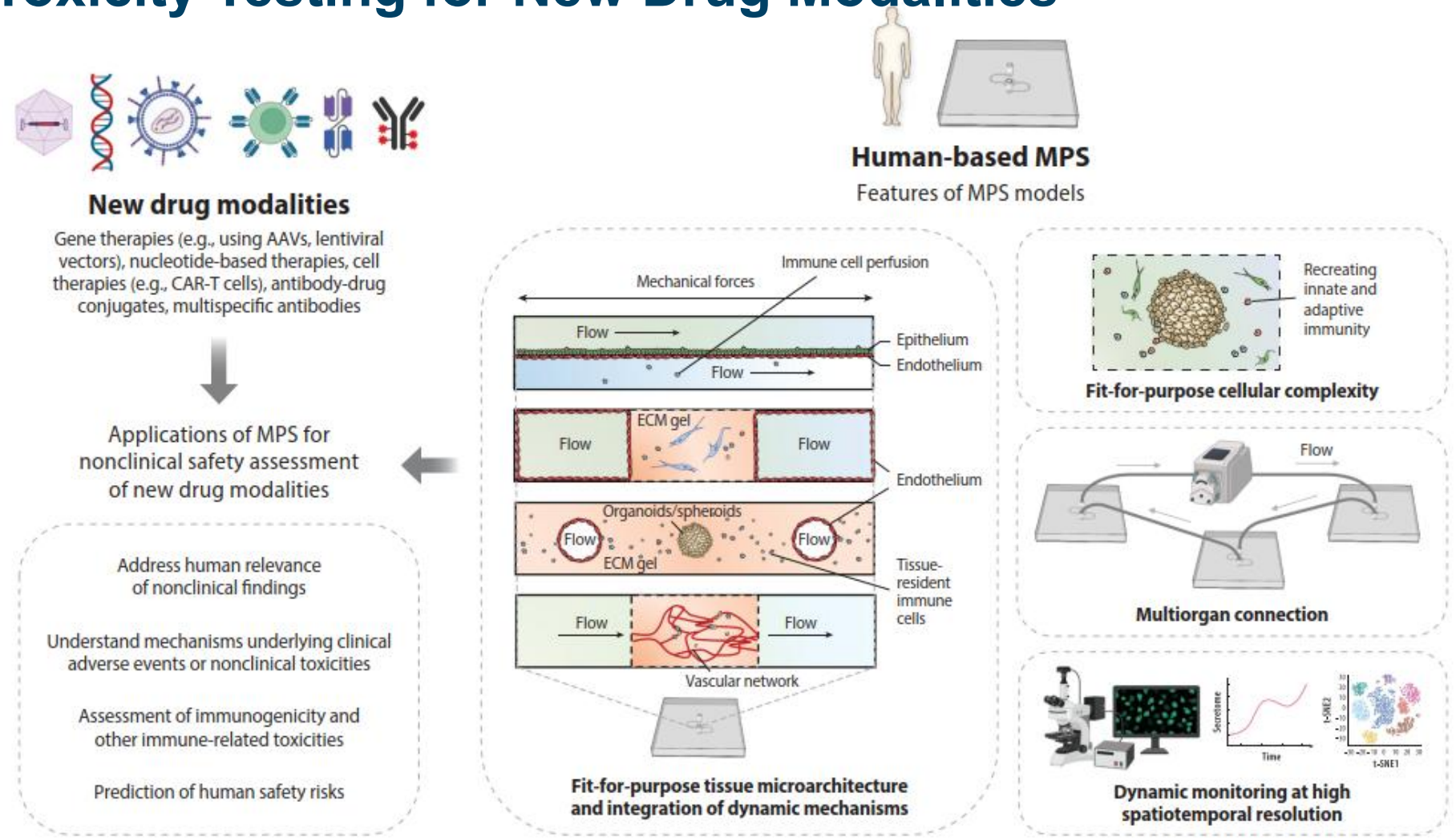


https://www.fda.gov/files/newsroom/published/roadmap_to_reducing_animal_testing_in_preclinical_safety_studies.pdf

Name	Mechanism of Action
Infliximab	TNF-α inhibitor (monoclonal mouse–human chimeric antibody)
Etanercept	TNF-α inhibitor (human form of TNF-α receptor fused with IgG)
Adalimumab	TNF-α inhibitor (monoclonal antibody)
Certolizumab	TNF-α inhibitor (Fab fragment of a monoclonal antibody)
Golimumab	TNF-α inhibitor (human monoclonal immunoglobulin antibody)
Rituximab	CD20 surface antigen antagonist (chimeric mouse/human monoclonal antibody)
Tocilizumab	IL-6 receptor antagonist (human monoclonal antibody)
Anakinra	IL-1 receptor antagonist (recombinant)
Abatacept	CTLA-4 antagonist (human fusion protein of the cell-surface marker CTLA-4 and immunoglobulin)
Ipilimumab	CTLA-4 blockade checkpoint inhibitor (human monoclonal antibody)
Nivolumab	PD-1 blockade checkpoint inhibitor (human monoclonal antibody)
Pembrolizumab	PD-1 blockade checkpoint inhibitor (humanized monoclonal antibody)
Cemiplimab	PD-1 blockade checkpoint inhibitor (monoclonal antibody)
Atezolizumab	PD-L1 blockade checkpoint inhibitor (humanized monoclonal antibody)
Avelumab	PD-L1 blockade checkpoint inhibitor (humanized monoclonal antibody)
Durvalumab	PD-L1 blockade checkpoint inhibitor (humanized monoclonal antibody)

Shah 2020,

Potential for the Use of Microphysiological Systems (MPS) in Toxicity Testing for New Drug Modalities

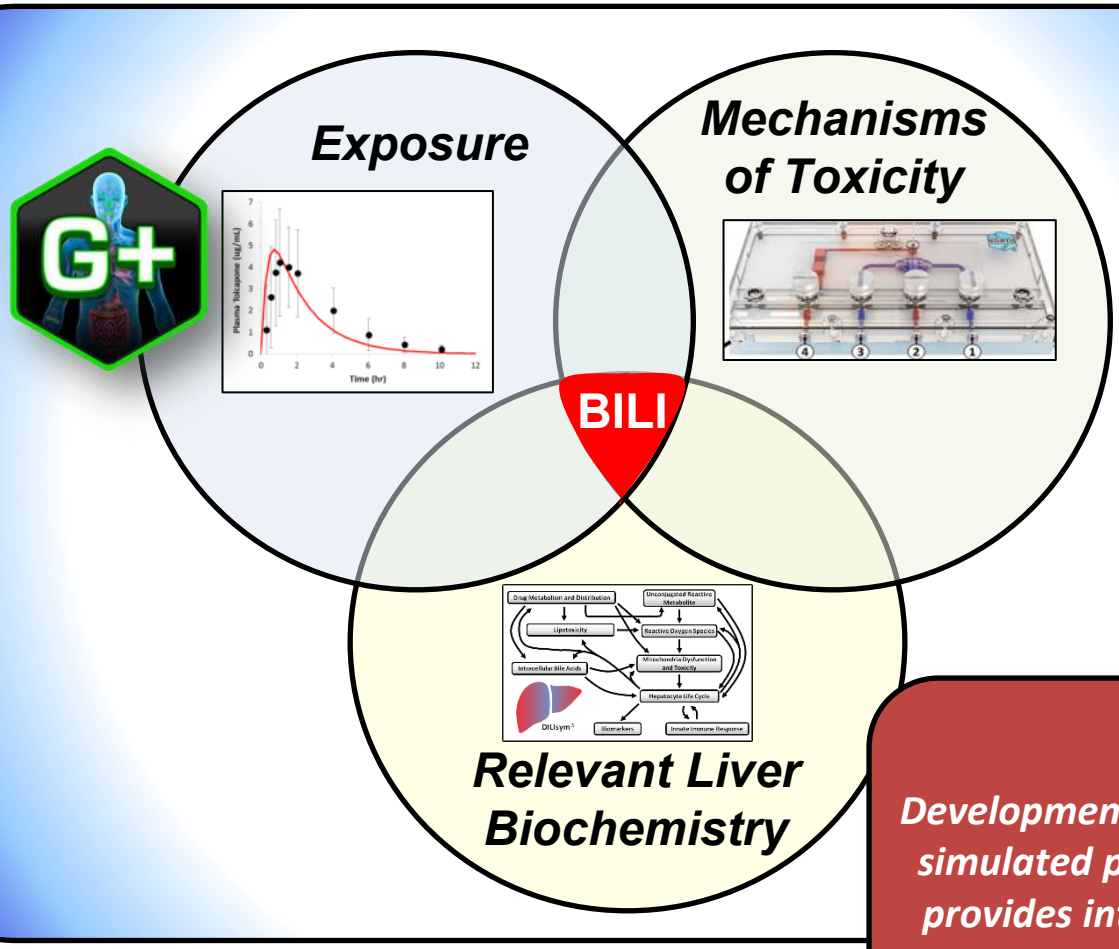


MPS include multiple cell types and increased physiologic relevance which may provide needed information for new drug modalities

Maulana 2025, PMID 39227343

Proof-of-Concept Efforts to Adapt QST Approaches to Bring Additional Mechanistic Context to Biologics NAM Data

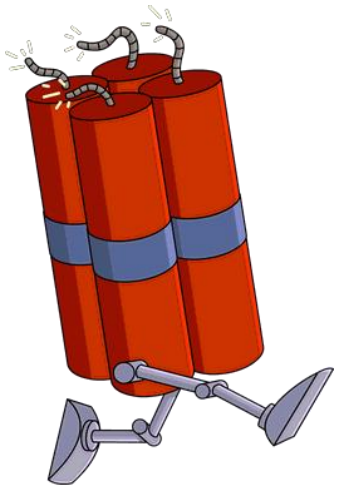
Predicted compound concentrations at site of toxicity using the biologics module in PBPK modeling software



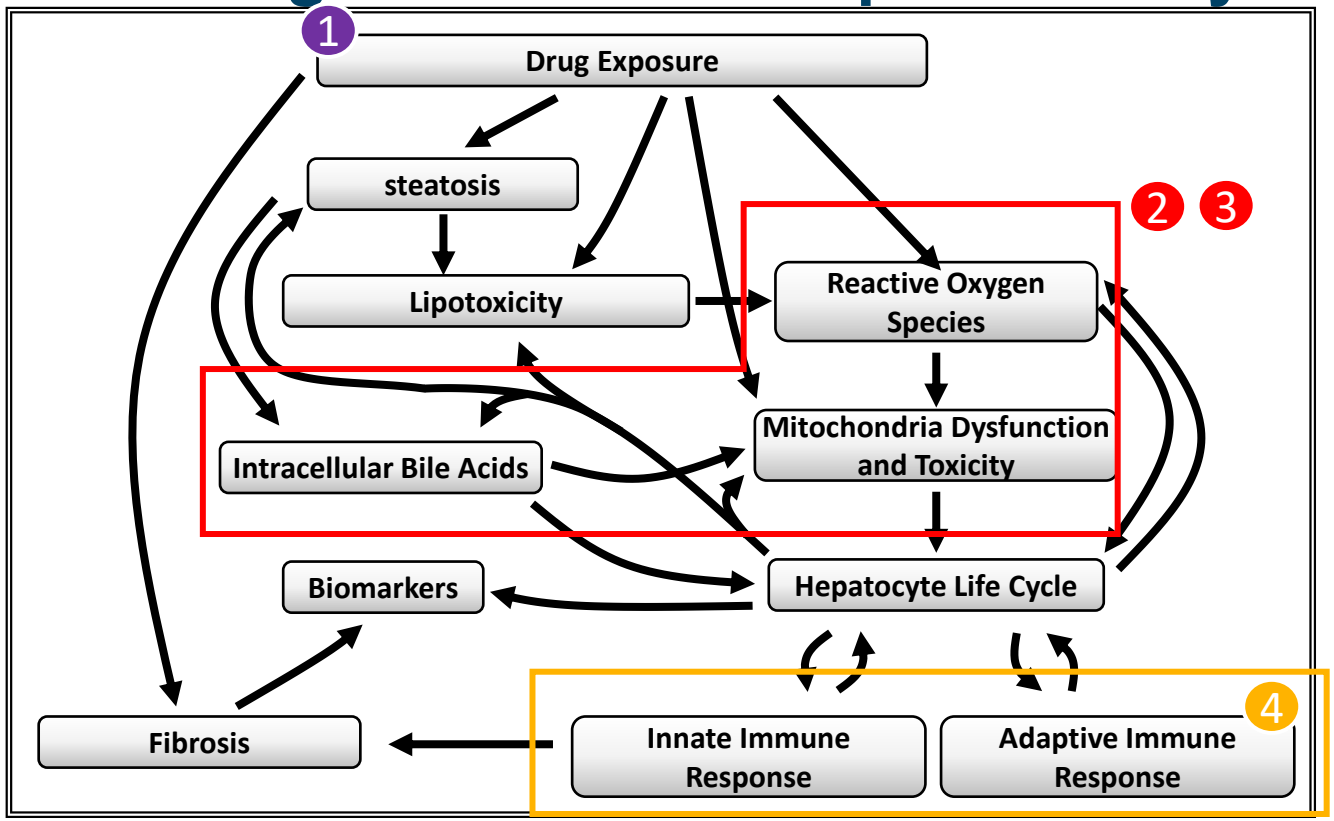
Toxicity mechanisms for exemplar mAbs and MPS data for proof-of-concept workflow development

Mechanistic representation of underlying biochemistry describing pathophysiology is foundation of QST models

Development and use of simulated populations provides inter-patient variability



BIOLOGXsym Workflow: A Staged Approach for QST Modeling of Biologics-Mediated Hepatotoxicity



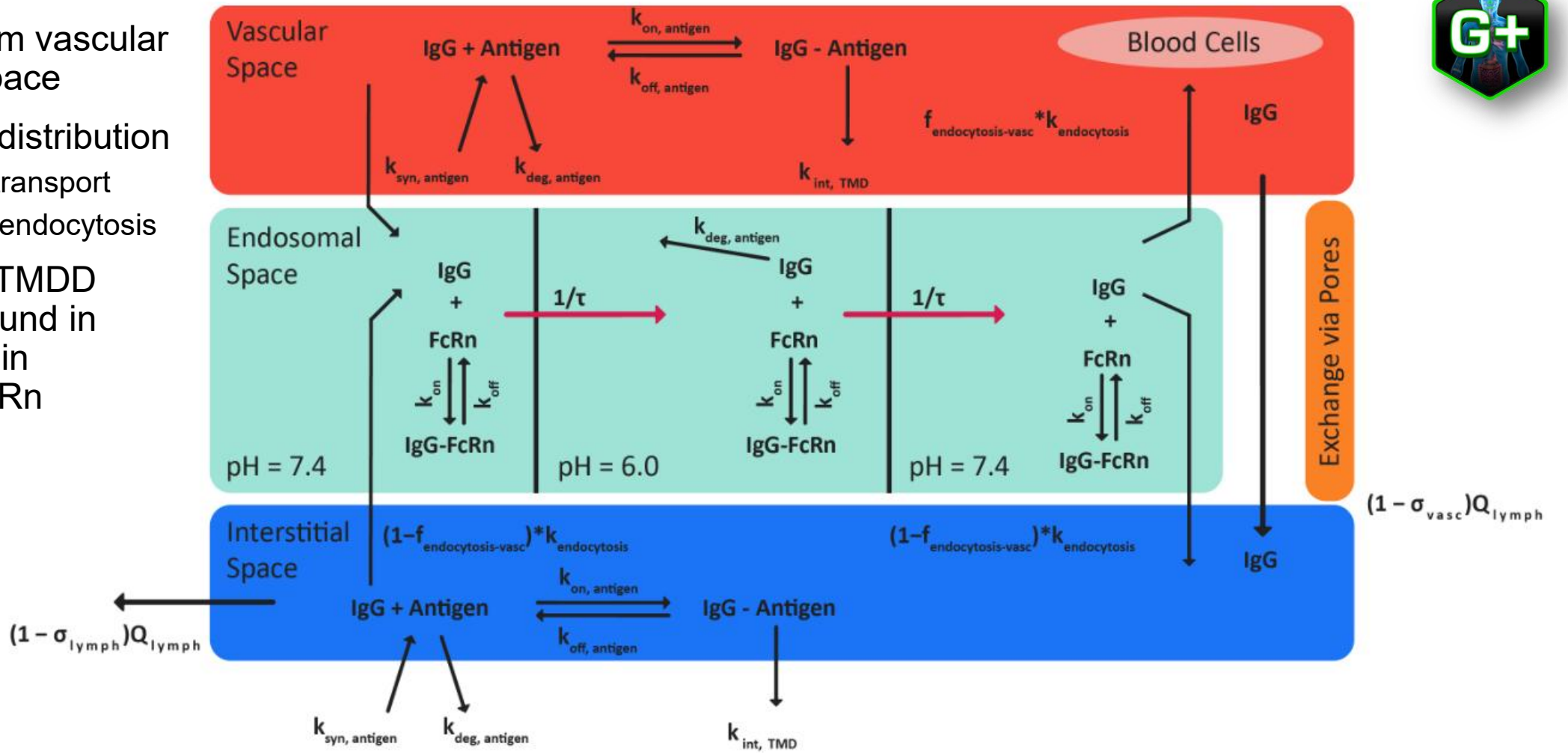
Compound	Direct hepatocyte stress mechanisms from LAMPS	Target-mediated mechanisms affecting hepatocytes
GGF2	BA, Mito	None
Tocilizumab	ROS	Inhibits IL-6 signaling
Infliximab	BA, Mito	Inhibits TNF-α signaling*
Ipilimumab	Mito	Increases effector CD8+ T cell proliferation, mediator production, and cytotoxicity*
Nivolumab	BA, Mito, ROS	Increases exhausted CD8+ T cell proliferation, mediator production, and cytotoxicity*
Bevacizumab	None	None

*Not included in current simulations yet

1. Develop and validate PBPK models
2. Identify direct hepatocyte stress mechanisms from microphysiological systems
3. Simulate hepatic responses based on direct hepatocyte stress signals
4. Simulate hepatic responses combining direct hepatocyte stress mechanisms and target-mediated mechanisms, if relevant, for inflammatory or adaptive immune systems

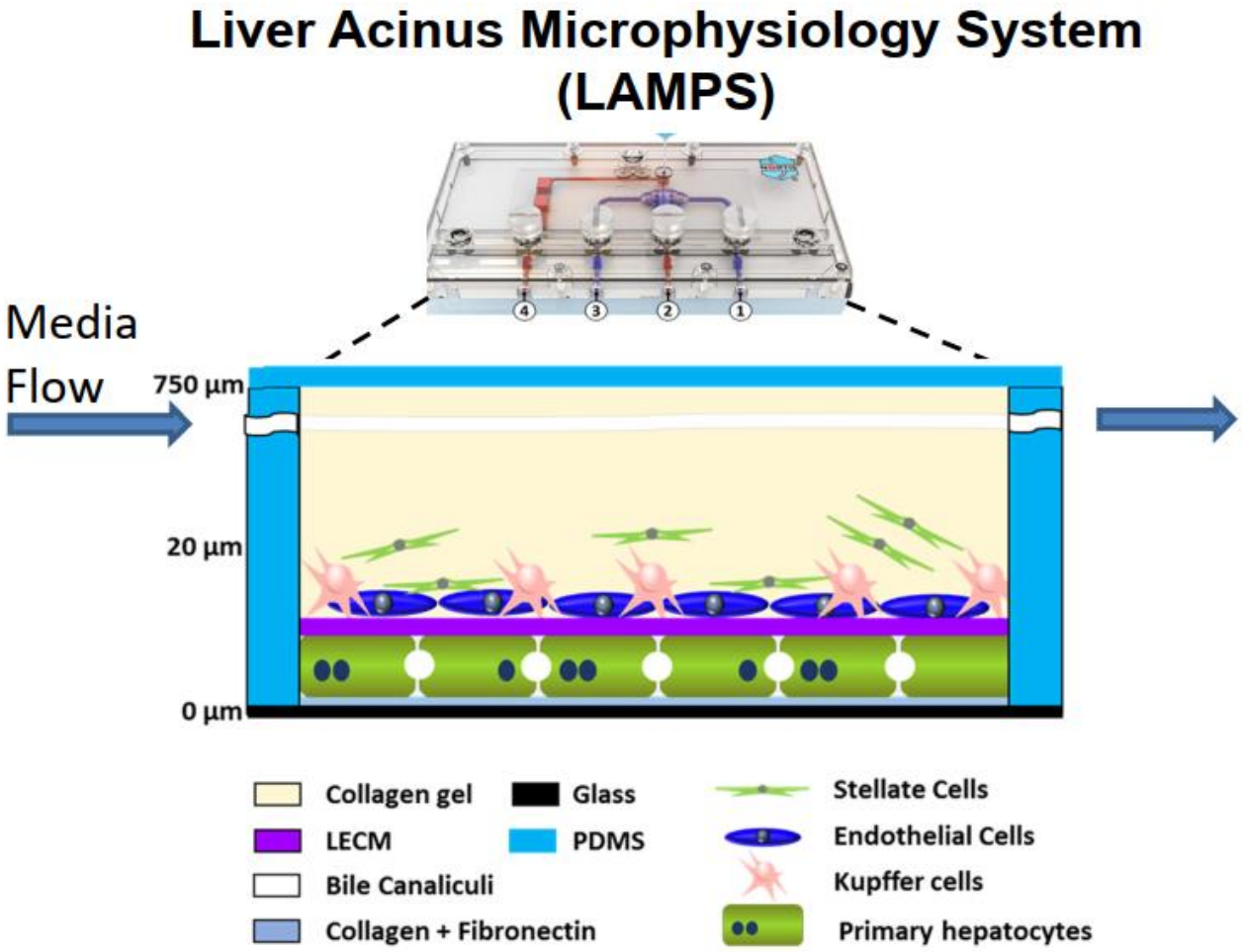
Biologics Exposure Paradigm Requires an Alternate Pharmacokinetic Representation (vs Small Molecules)

- Distribution from vascular to interstitial space
- Two modes of distribution
  - Convective transport
  - Fluid phase endocytosis
- Clearance via TMDD (membrane-bound in tissue, soluble in circulation), FcRn dissociation



Liver Acinus MPS (LAMPS) for Analysis of mAb Exposure Related Mechanisms of Toxicity

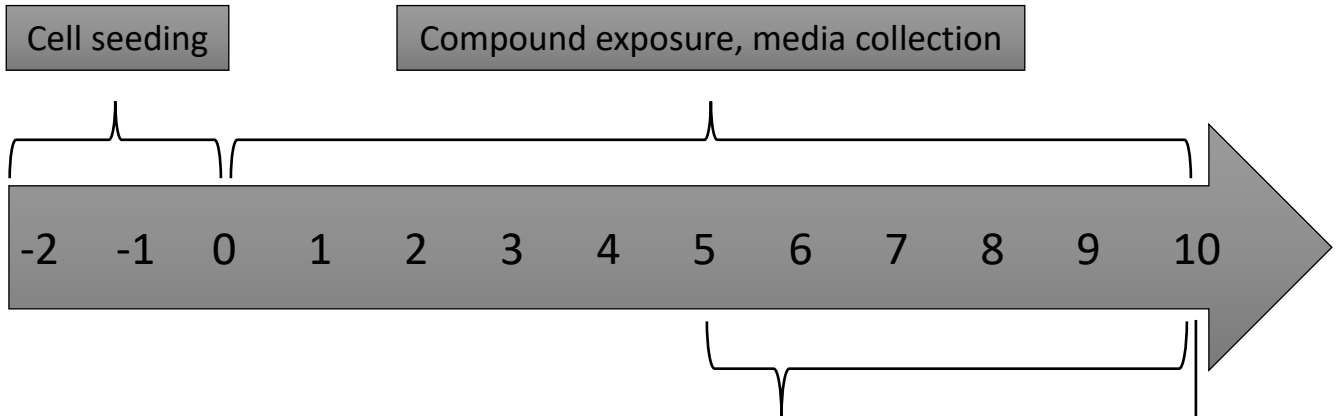
- LAMPS model includes 4 cell types and flow (5 µL/h to create hepatic zone 3 oxygen tension)
  - Primary hepatocytes, LX2 stellate cells, THP-1 Kupffer-like cells, primary liver sinusoidal endothelial cells (LSECs)
- Cell- and media-based analysis including
  - Intracellular lipid accumulation, albumin, blood urea nitrogen, lactate dehydrogenase, CCL2, IL-1β, IL-6, TNF-α, IL-10, bile acid efflux (GCDCA, TCA), oxidative stress, metabolomics

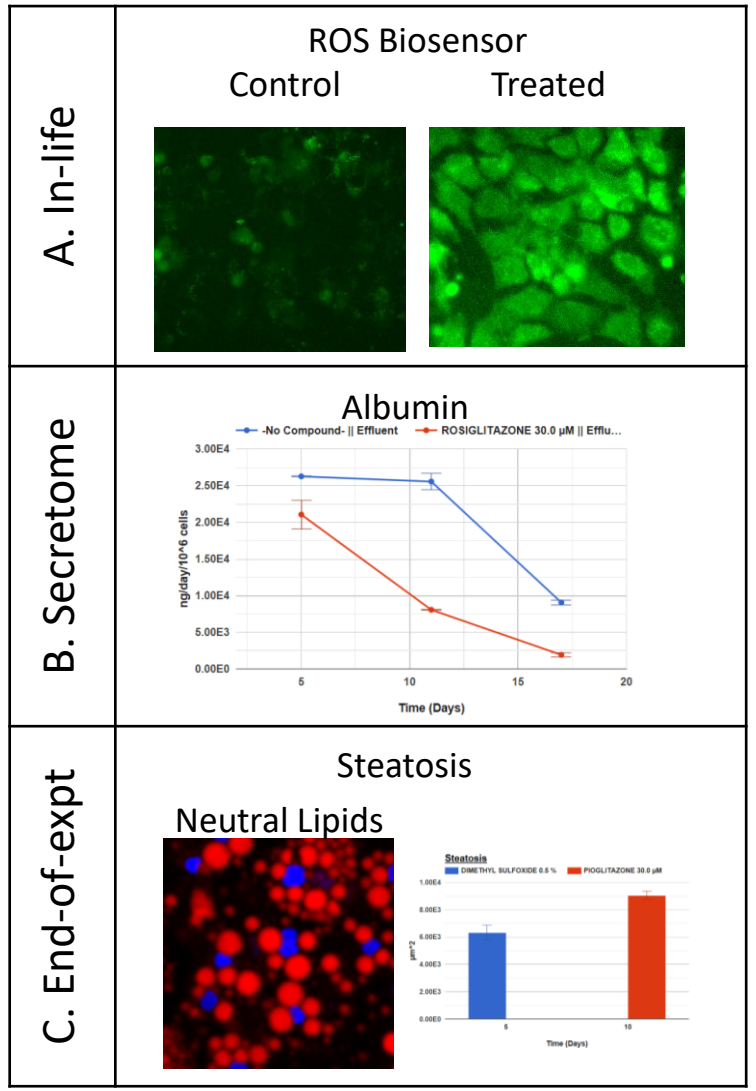


Beaudoin 2023, PMID 37298645

Experimental Design Included Concentration- and Time-Dependent Measures

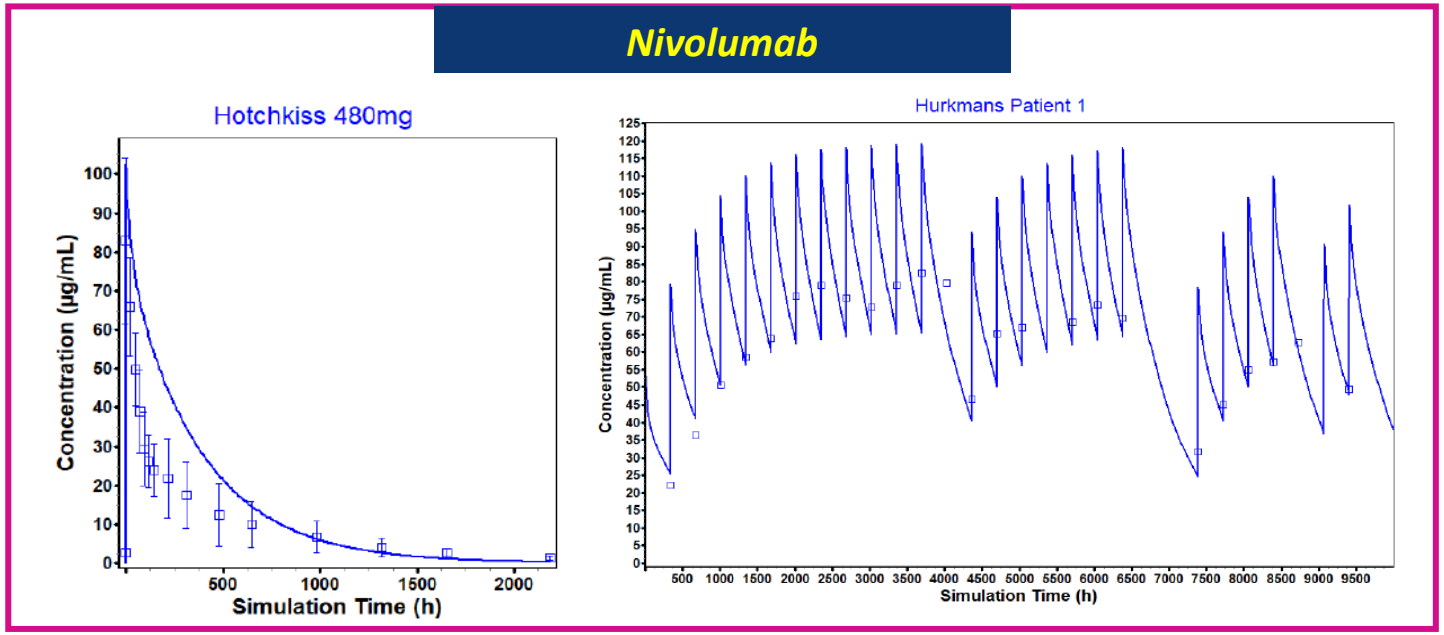
- 2-3 selected concentrations based on measured C_{max}
- Treatment and measurements over 10-day culture
  - Live cell-based measurements
  - Secretome measurements
  - End-of-experiment measurements





PBPK Model of Nivolumab Was Developed Using Biologics Module within GastroPlus

- A PBPK model of nivolumab was optimized and validated using publicly available clinical PK data
  - IV administration, single and multiple dosing
  - TMDD captures impact of PD-1 binding on nivolumab PK
  - Predicted hepatic interstitial concentration-time profiles of nivolumab drive drug-effects on hepatocytes in BIOLOGXsym (not shown)

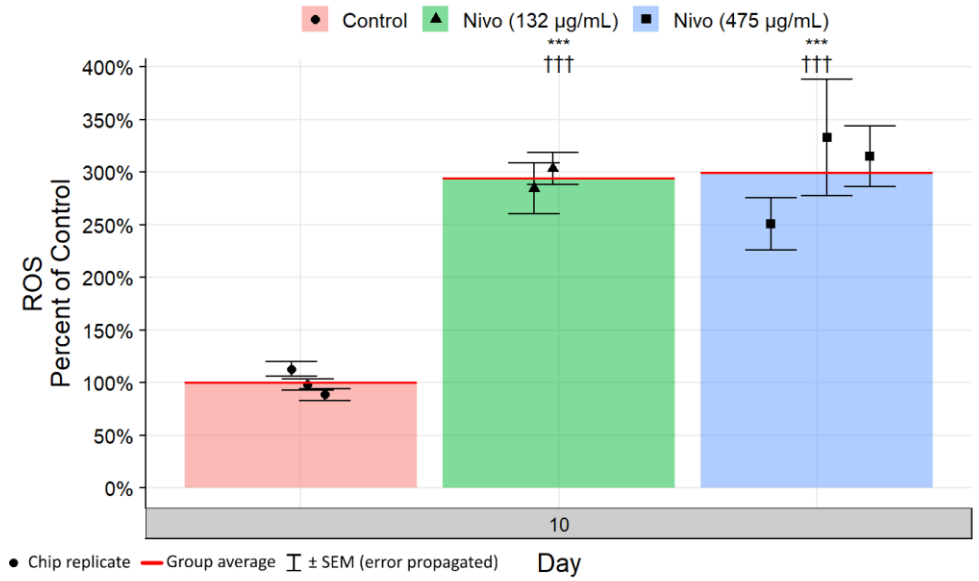


Vallejo et al., Pharmaceutics (2025)

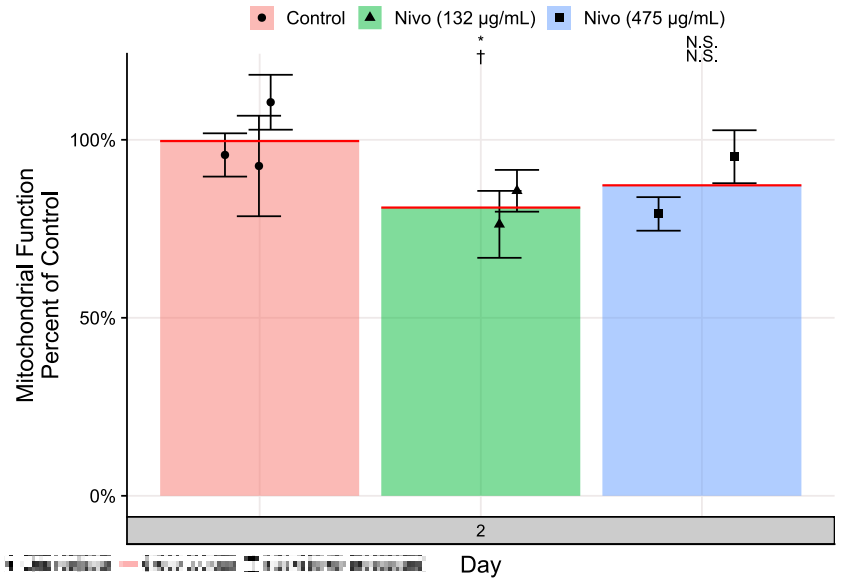
LAMPS Assays Show Hepatocyte Stress Signals for Nivolumab

- LAMPS experimental outputs demonstrate early hepatocyte stress signals and mechanisms for nivolumab
- Nivolumab significantly increased ROS and decreased mitochondrial function and bile efflux

Reactive Oxygen Species (ROS)



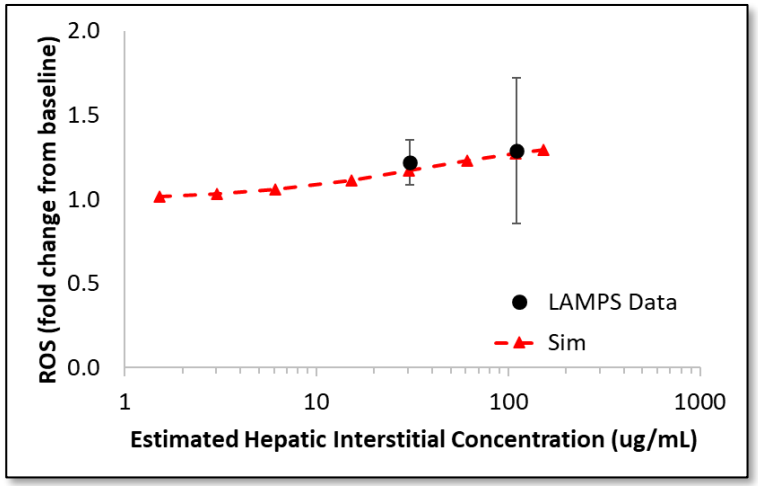
Mitochondrial Toxicity



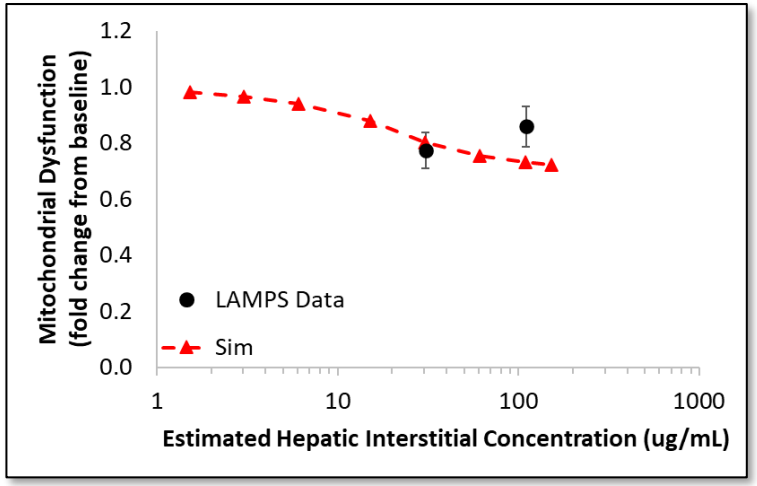
LAMPS Data Indicate Nivolumab Induces Oxidative Stress While Reducing Mitochondrial Function and Bile Acid Efflux

- Nivolumab exposure at two concentrations 0.92 and 3.30 µM provided consistent evidence of oxidative stress, mitochondrial dysfunction, and reduced bile acid efflux
- Parameterization of measured changes relative to control chips were incorporated in BIOLOGXsym
- Parameterized model combined with nivolumab PBPK-predicted liver exposure and simulated inter-individual variability to predict population-level hepatotoxicity

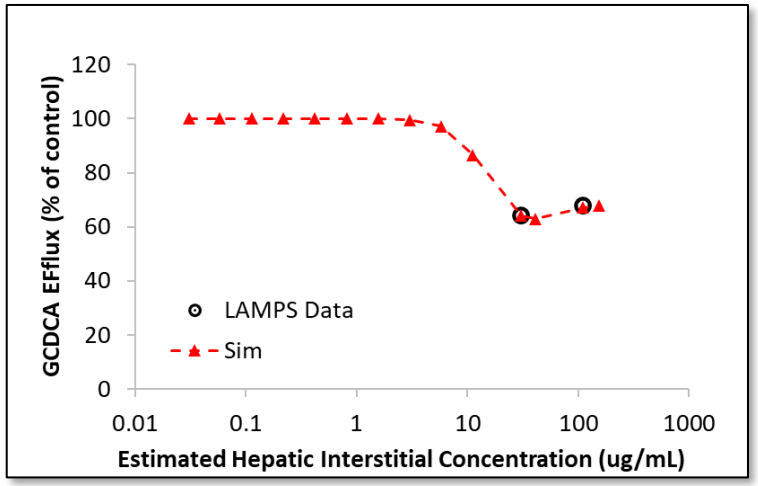
Oxidative stress



Mitochondrial dysfunction



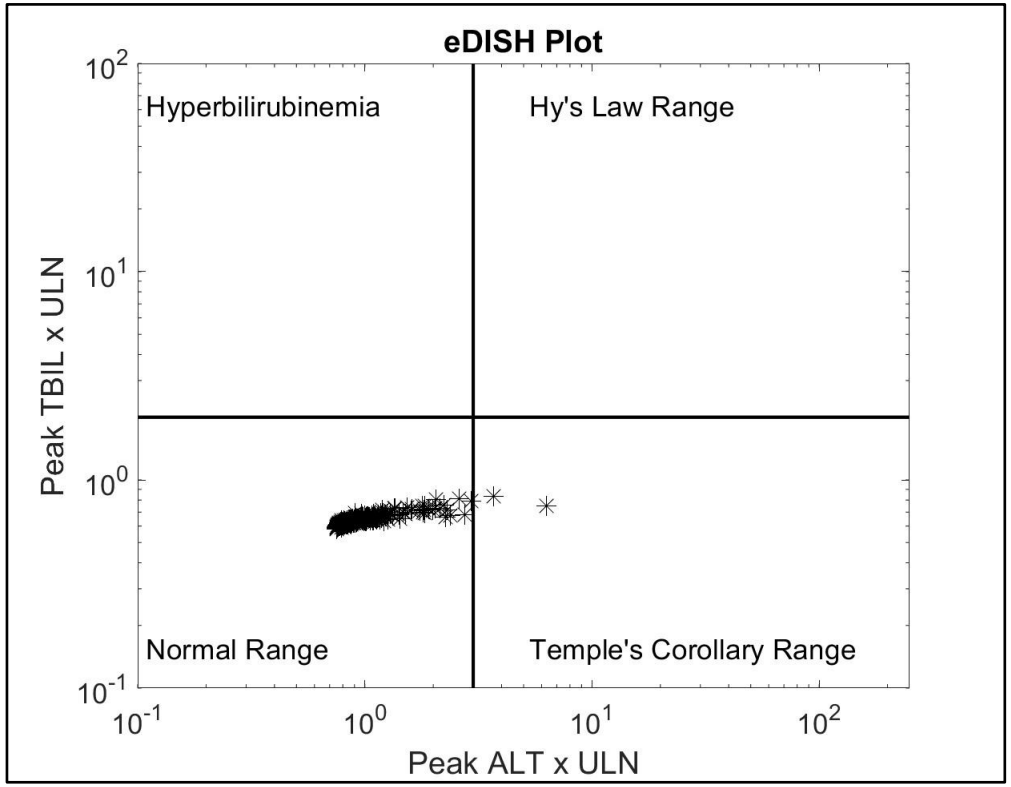
Bile acid efflux



Yang 2026, ASCPT (Denver, CO)

Simulations Integrating Nivolumab Exposure, LAMPS Data, and Inter-Subject Variability Predict Mild Hepatotoxicity

- Mild hepatotoxicity predicted on simulation of 480 mg IV q4w over 12 weeks in an N=285 population with normal livers
- Results overpredict mild hepatotoxicity and underpredict more serious hepatotoxicity events
  - 2% Gr 1-4, 0.5% Gr 3-4 in phase 3 studies (Zarrabi 2018, PMID 29539626)
- Results do not account for immune activation events, e.g., T cell, cytokine, complement contributions

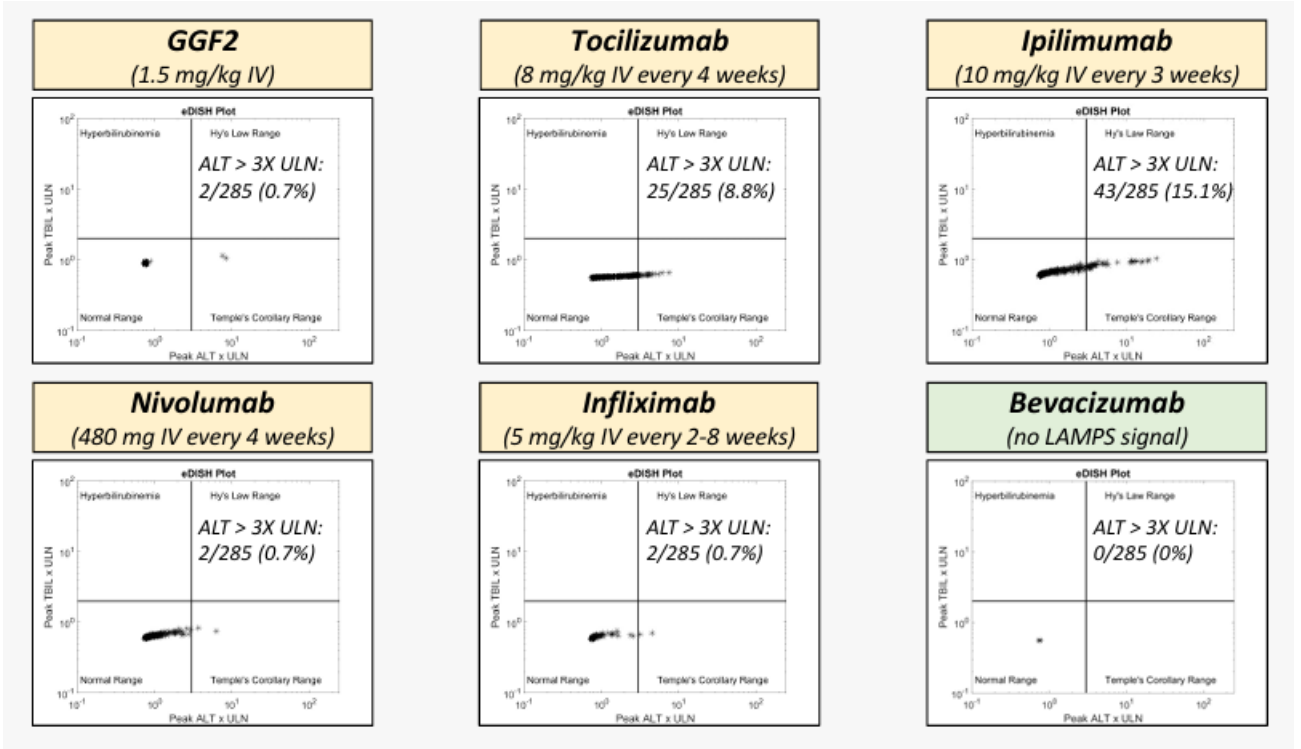


ALT > 1x ULN: 89/285 (31.2%)
ALT > 3x ULN: 2/285 (0.7%)

Yang 2026, ASCPT (Denver, CO)

BIOLOGXsym Predicts Toxicity for Other Biologic Compounds With Liver Liabilities

- BIOLOGXsym workflow used on six compounds with varying levels of liver liabilities
  - GGF2, tocilizumab, ipilimumab, nivolumab, and infliximab were positive controls
  - Bevacizumab was a negative control



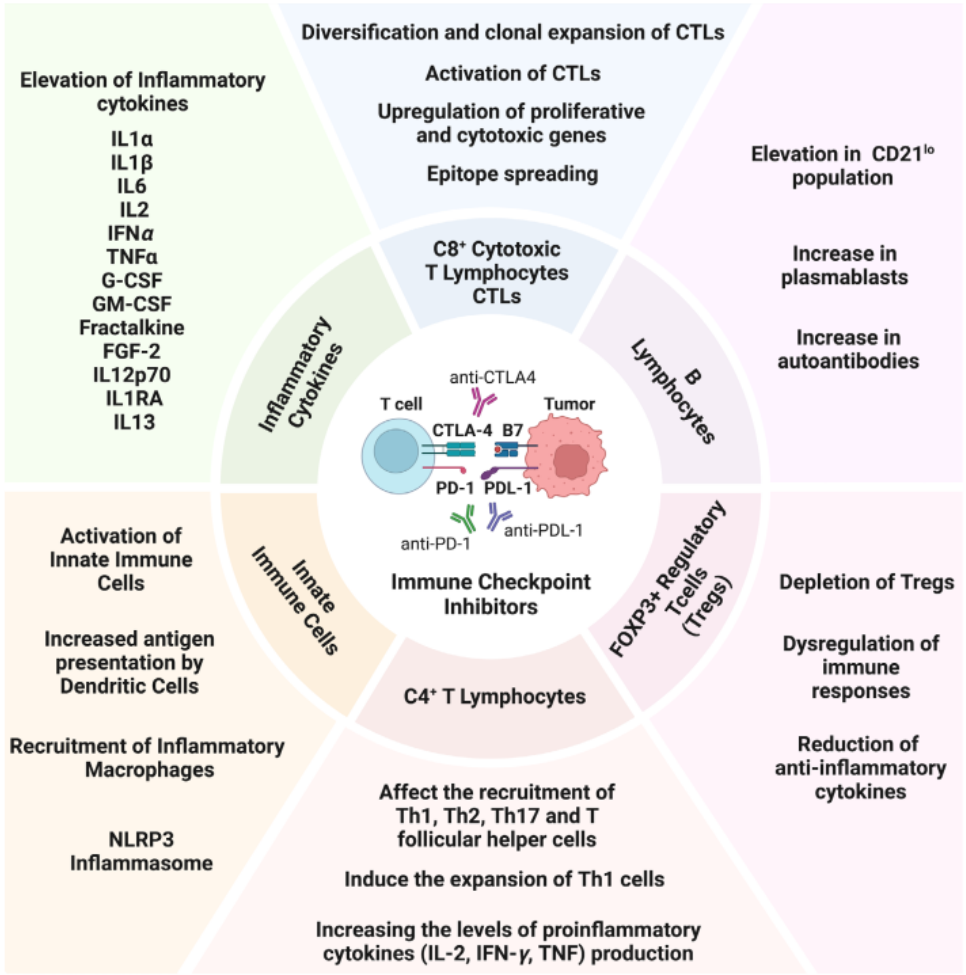
Beaudoin 2026, QSPe (Leiden, Netherlands)

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- Novel biologic-induced toxicity mechanisms
- Next steps: siRNA drugs and other liver-on-a-chip systems

Beyond the Mechanisms Evaluated, Nivolumab-Mediated Activation of T cells may Contribute to Observed Liver Injury

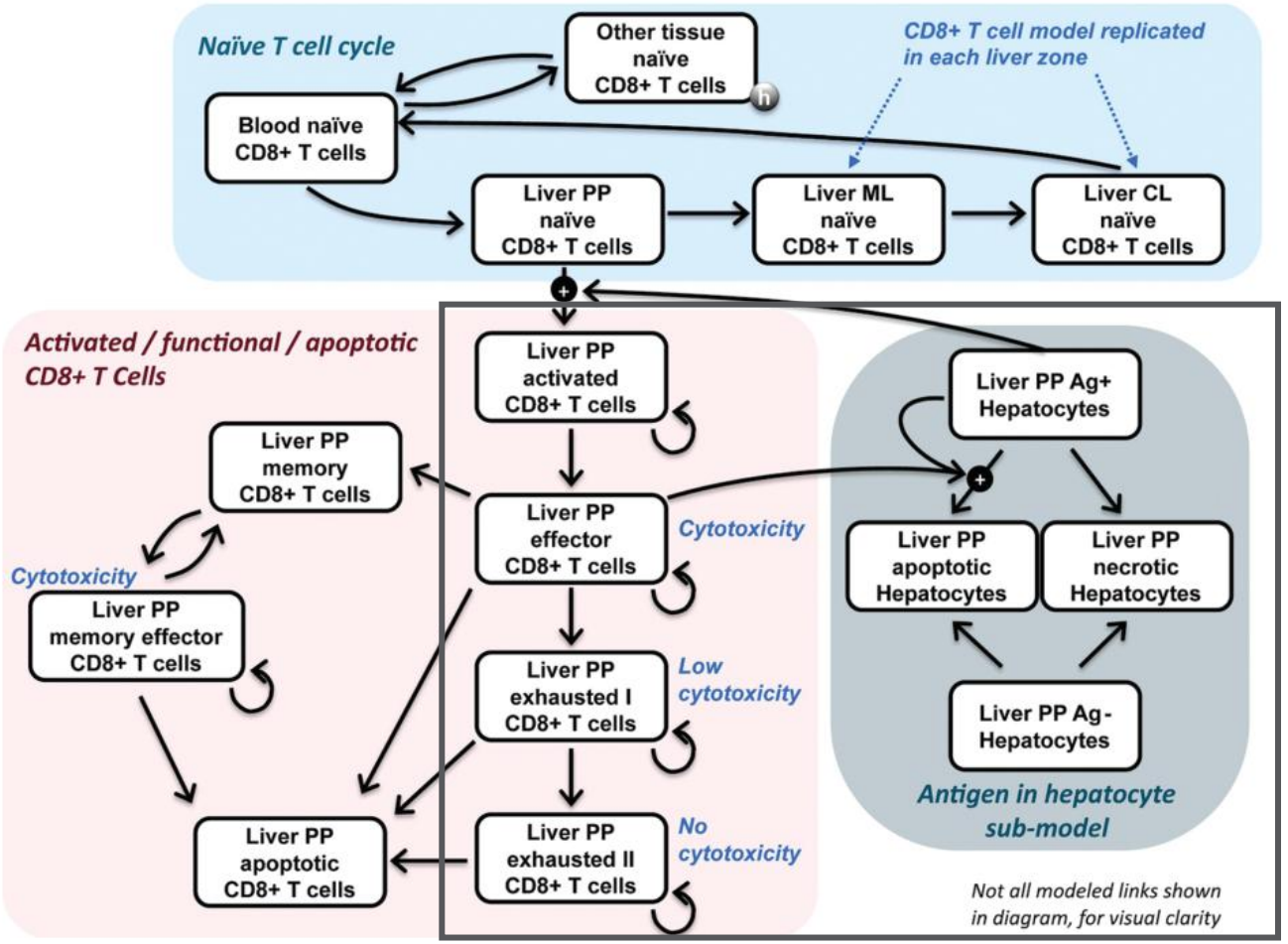
- ICIs have diverse effects on the immune system, many of which could influence liver injury
- One leading hypothesis suggests that tumor killing releases neo-antigens that are involved in immune-related adverse events
- Potentially relevant hypotheses:
  - Neo-antigens released that share features with liver antigens
  - De novo T cell responses to neo-antigens and/or similar liver antigens
  - ICI-activated T cells that had previously responded to liver antigens (and been down-regulated)



Dara 2025, PMID

T cell Sub-Model Developed in DILIsym for the Investigation of De Novo Drug-Specific T cell Mediated DILI

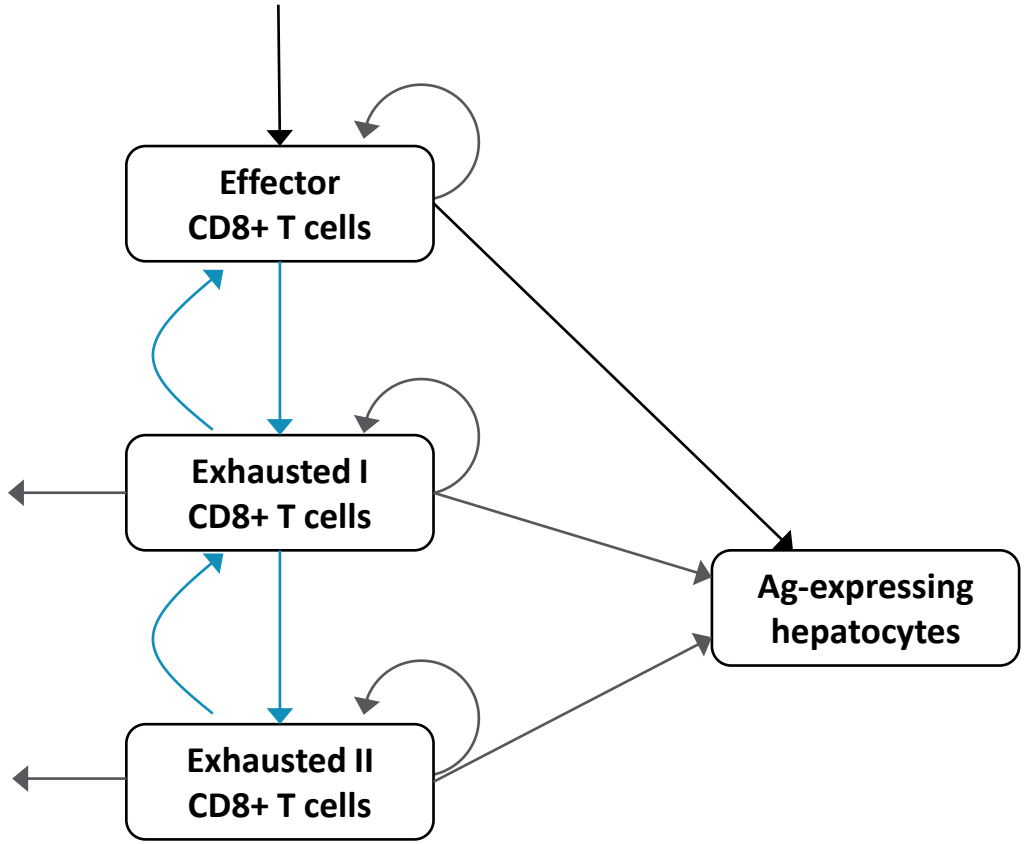
- T cell sub-model, focused on de novo generation of CTL response to antigen expressed by hepatocytes, originally developed for DILIsym
  - Developed around experimental antigen and amodiaquine
- Sub-model repurposed to consider hypotheses on immune-related adverse events following ICI treatment



Clemens 2025, PMID 40324052

Consideration of Two Hypotheses for CTL-Mediated Liver Injury Following Nivolumab Treatment

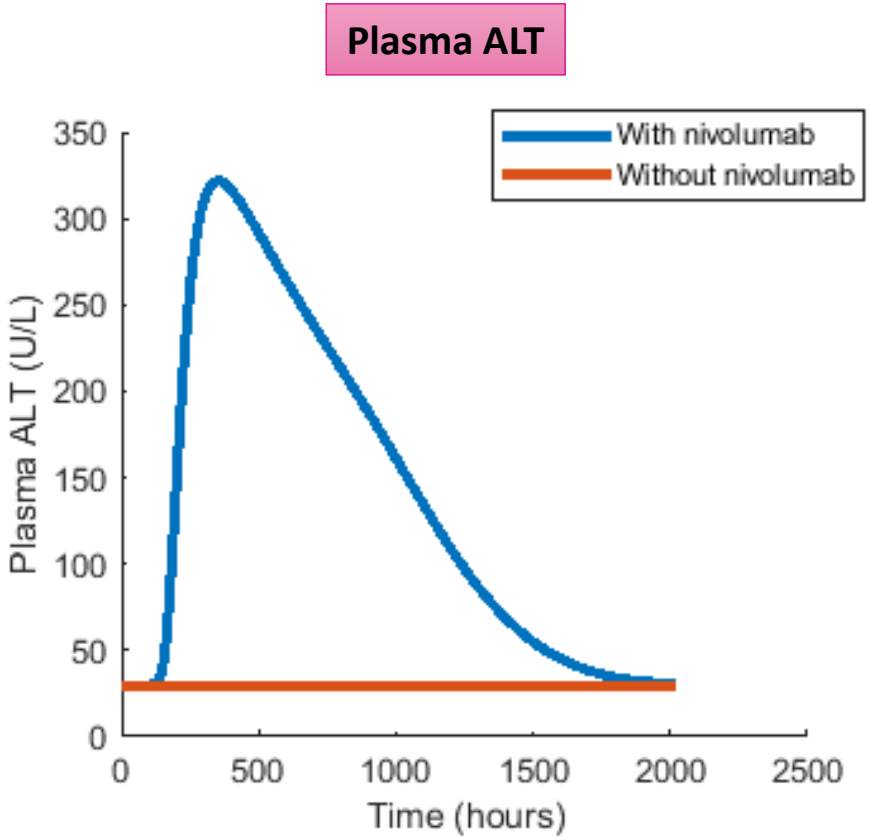
- To explore the potential role of nivolumab activation of exhausted T cells in liver injury, two scenarios are considered
  - **Scenario 1**: on nivolumab exposure, exhausted T cells revert to a fully functional effector T cell state, capable of killing Ag-expressing hepatocytes
  - **Scenario 2**: on nivolumab exposure, exhausted T cells regain some functionality and are able to kill Ag-expressing hepatocytes
- T cell simulations, including integration with LAMPS data ongoing



Proof-of-Concept Simulations Show ALT Elevations after Nivo-Mediated Changes in T Cell Dynamics

4

- Preliminary simulations of ALT elevations for individual including nivolumab effects (blue) vs without nivolumab effects (red)
  - Nivolumab representation includes increased proliferation, decreased apoptosis, and increased cytotoxicity of exhausted CD8+ T cells
- Key assumptions
  - Nivolumab represented as constant effect at start of simulation, i.e., no exposure dependence in preliminary simulations
  - Nivolumab affects antigen-experienced exhausted CD8+ T cells
  - No new activation of naïve CD8+ T cells
  - Liver tolerance compromised
  - Antigen-experienced exhausted T cells migrate to liver
  - Antigen was present in the liver at a constant level prior to nivolumab administration



Nivolumab Representation Evaluated in SimPops Expressing T cell Variability

- SimPops (n=500) generated with variability in key CD8+ T cell baselines and dynamics
  - SimPops customized to evaluate nivolumab mechanism
- Key assumptions
  - Nivolumab represented as constant effect at start of simulation, i.e., no exposure dependence in preliminary simulations
  - Nivolumab affects antigen-experienced exhausted CD8+ T cells
  - No new activation of naïve CD8+ T cells
  - Liver tolerance compromised
  - Antigen-experienced exhausted T cells migrate to liver
  - Antigen was present in the liver at a constant level prior to nivolumab administration

Parameter	Range
Avidity	0,1
Regulatory feedback IC50	1, 1000
Liver exh1 CD8+ T cells at baseline relative to naive	1, 1000
Liver exh2 CD8+ T cells at baseline relative to naive	1, 1000
Fraction HCs expressing Ag	0.01, 0.5
Exh1 & Exh2 proliferation scalar	0.066, 0.11
Exh1 & Exh2 apoptosis scalar	0.1, 0.2
Exh1 & Exh2 cytotoxicity scalar	0.01, 1
Exh1 to Exh2 differentiation rate	0.01, 1

Peak Simulated Plasma ALT Elevations Consistent with Peak Observed Plasma ALT Elevations

4

- Preliminary simulations of nivolumab effects on T cell dynamics demonstrate variability in response
  - Variability in underlying T cell dynamics and nivolumab effects captured in simulated population
  - Peak simulated ALT ranged from no elevation (30 U/L baseline) to more than 700 U/L
- Magnitude of ALT elevations simulated captures range of clinically observed ALT elevations
- Future simulations of nivolumab will implement time-dynamic exposure and exposure-dependent effects on CD8+ T cell dynamics

Reference	Maximum observed ALT value (U/L)	Time point maximum ALT elevation observed after nivo start
Matsubara 2018	785	~51 weeks
Imoto 2019	1198	~14 days
Imoto 2019	157	~360 days
Imoto 2019	167	~56 days
Imafuku 2017	822	~34 weeks
Wuyts 2021	663	~31 weeks
Simulation	**30-736**	**N/A***

*Preliminary simulations do not include exposure dynamics that would significantly impact timing

Tocilizumab (TCZ) Associated with Mild Liver Safety Signals Although Infrequent Serious Events have been Reported

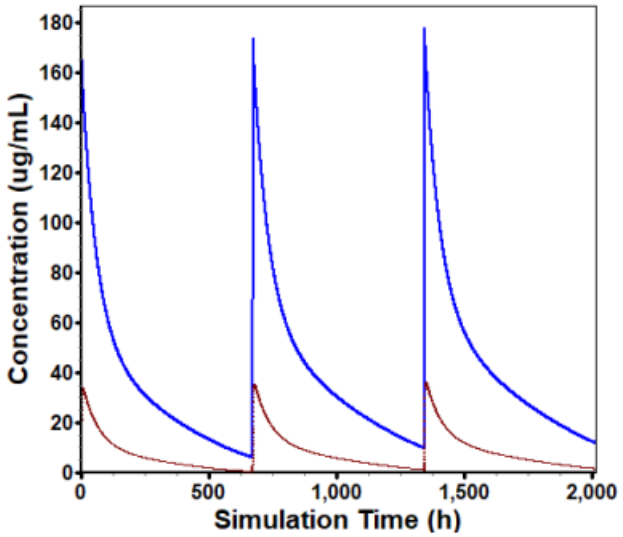
- TCZ is a monoclonal antibody that binds IL-6R
- Across multiple clinical trials in rheumatoid arthritis (RA) patients, mild ALT elevations with TCZ commonly observed
- Clinically significant (i.e., ALT>3x ULN) were observed less frequently
- Serious hepatotoxicity has been reported in a few case studies (e.g., Anger 2017, PMID 28575416)

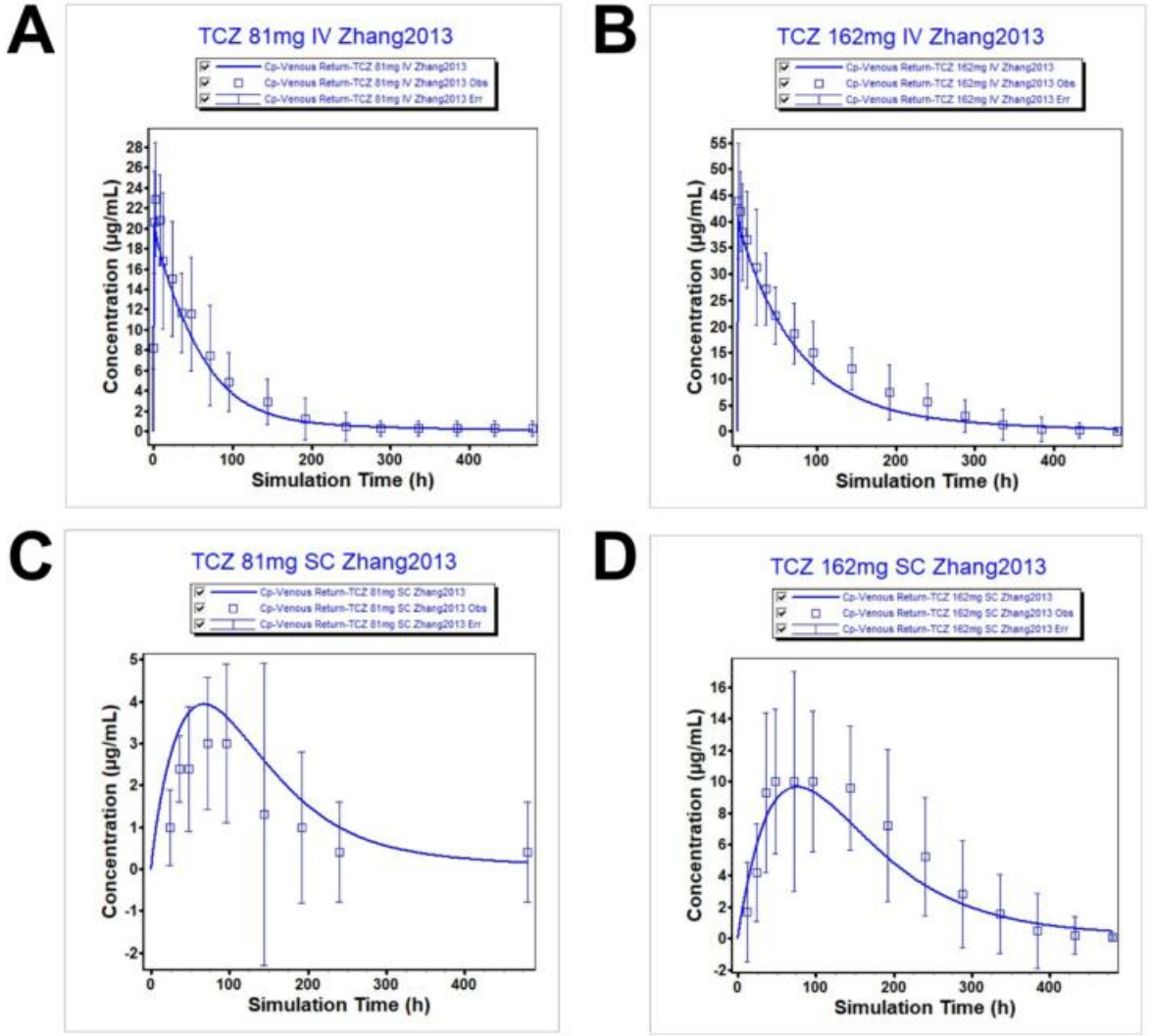
Patients	Treatment	Liver Safety	Reference
RA (n=288)	8 mg/kg q4w	33.8% >1x ULN ALT 1.9% >3x ULN ALT	Schiff 2011†, PMID 21884601
RA (n=774)	4 mg/kg q4w	42.8% >1x ULN ALT 4.0% >3x ULN ALT	
RA (n=1582)	8 mg/kg q4w	45.9% >1x ULN ALT 4.3% >3x ULN ALT	
RA (n=348)	162 mg SC q2w 8 mg/kg IV q4w	26.3% >1x ULN ALT (TCZ SC) 4.3% >3x ULN ALT (TCZ SC)	Ogata 2014, PMID 25834203
RA (N=437)	162 mg SC q2w	32.7% >1–3x ULN ALT 2.0% >3x ULN ALT	Kivitz 2014, PMID 24942540

† meta-analysis of five phase 3 trials

TCZ Pharmacokinetic (PK) Representation in the Biologics Module of GastroPlus

- TCZ PBPK model optimized to single dose data given IV or SC
- Model validated against reported repeat dosing summary statistics, AUC, C_{max}, C_{trough} (not shown here)
- Model then used to predict liver concentrations for TCZ 8 mg/kg, q4w

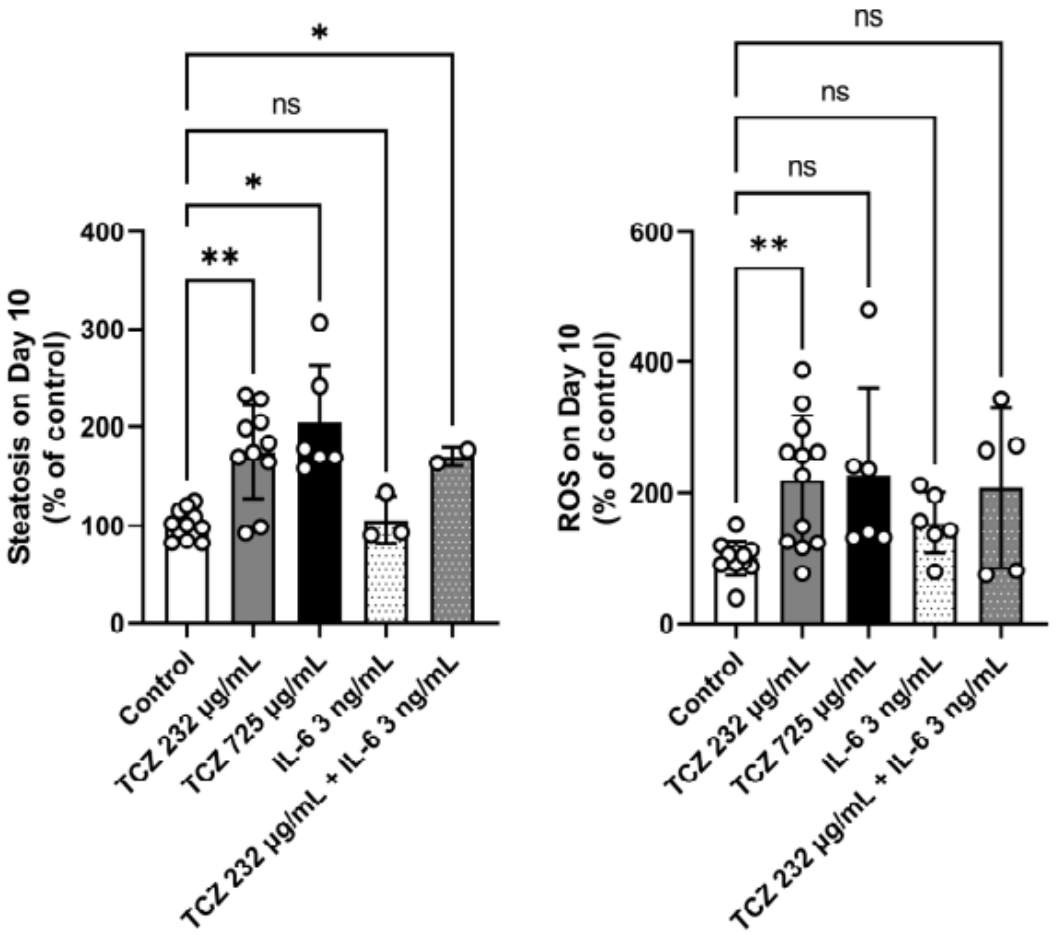




Beaudoin 2023, PMID 37298645

LAMPS Data Indicated the Potential for TCZ-Driven Steatosis and Oxidative Stress

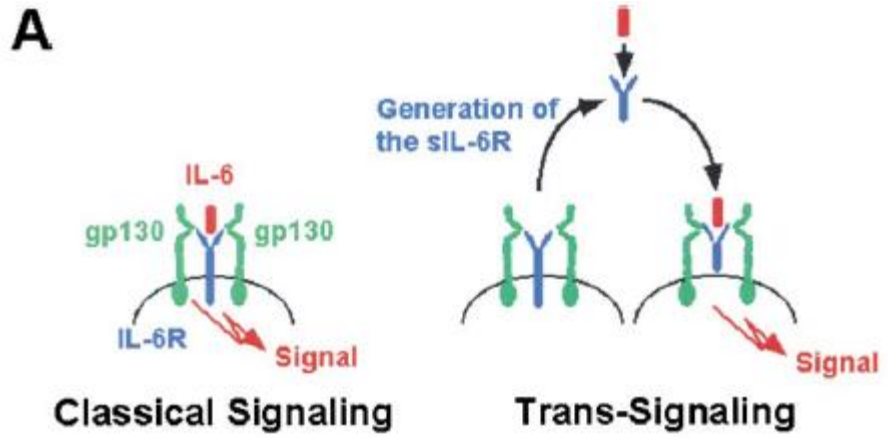
- Concentration- and time-dependent increases observed in fat accumulation (steatosis) and oxidative stress (ROS)
  - TCZ concentrations represent C_{max} associated with 8 mg/kg dosing and 3x C_{max}
  - Logistic constraints on the number of different concentrations that could be tested
- Co-administration of TCZ and IL-6 did not alter signal but does not rule out that effects were downstream of IL-6 signaling
- Inclusion of TCZ-mediated steatosis and oxidative stress as plausible mechanisms of toxicity



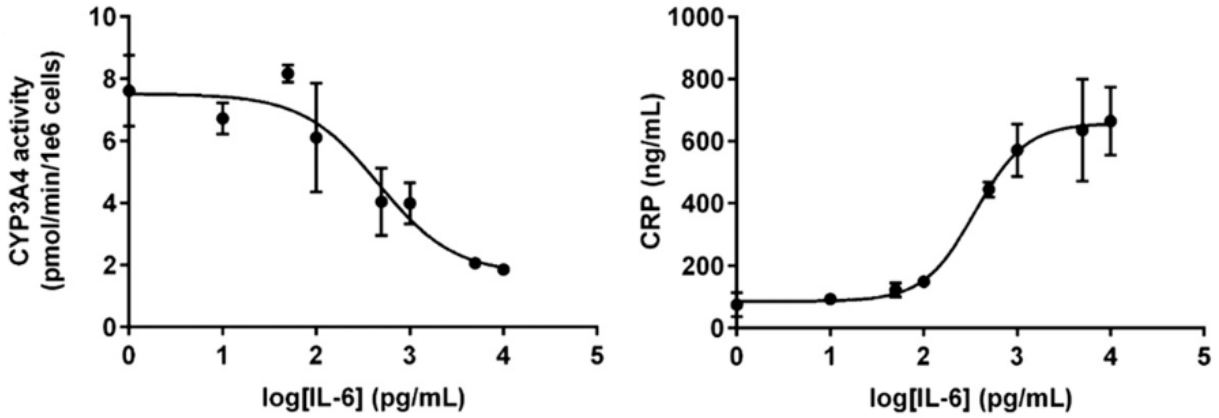
Beaudoin 2023, PMID 37298645

Key Features of IL-6 Signaling and Function Modeled for TCZ Representation

- IL-6 signaling, which occurs via membrane-bound gp130 can occur via classic or trans-signaling
  - Classic: IL-6 binds the membrane-bound receptor and signals via membrane-bound gp130
  - Trans: the IL-6-sIL-6R complex binds the membrane-bound gp130
- Endogenous IL-6 production by macrophages, LSECs, PMNs, HCs
  - sIL-6R by membrane shedding
- Besides role in inflammation, IL-6 affects HCs
  - CRP production, CYP expression, proliferation, bile acid efflux transporter expression



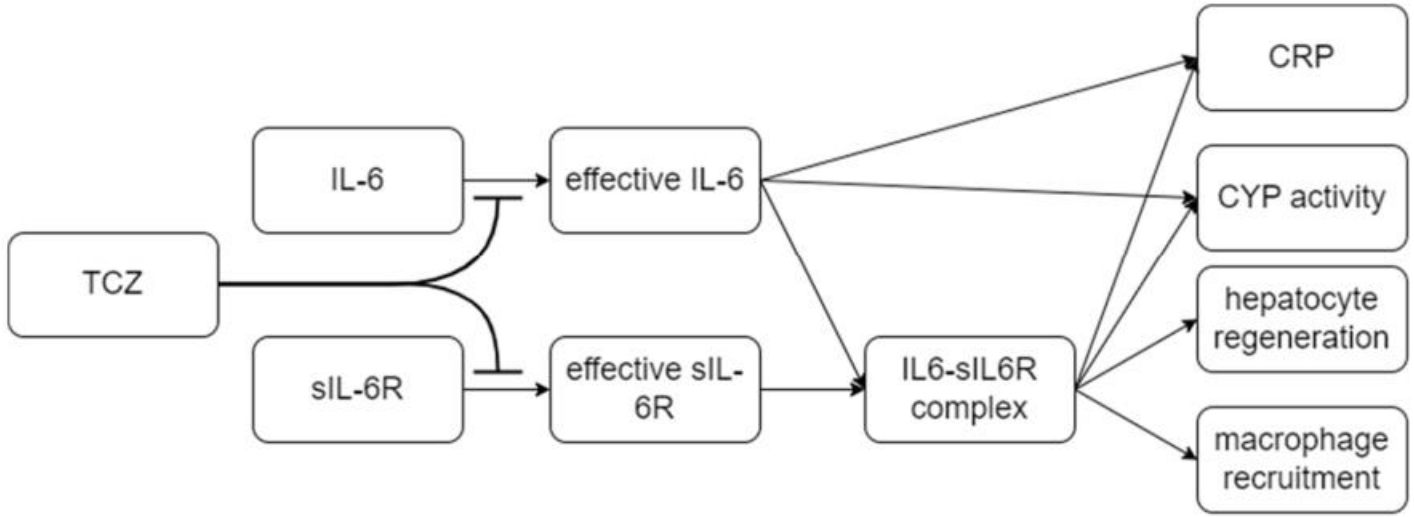
Rose-John 2004, PMID 14738759



Long 2016, PMID 27621203

Modeled IL-6 Representation Includes Both Classic and Trans-IL-6 Signaling for Key Liver Processes

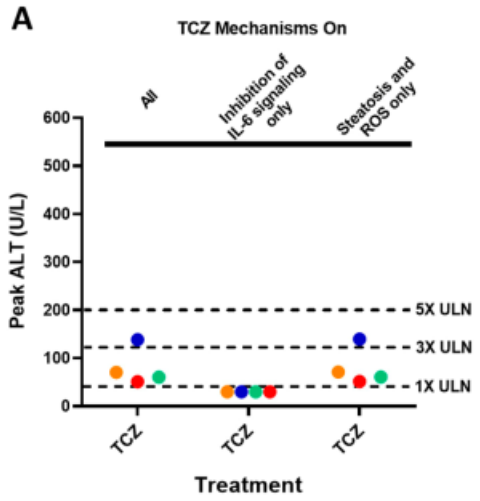
- IL-6 effects include
  - Increased CRP release
  - Suppression of CYP activity (CYP2E1, CYP3A4)
  - Increased hepatocyte regeneration
  - Increased monocyte/macrophage recruitment
- By antagonizing the IL-6R, TCZ reduced effective classic and trans IL-6 signaling

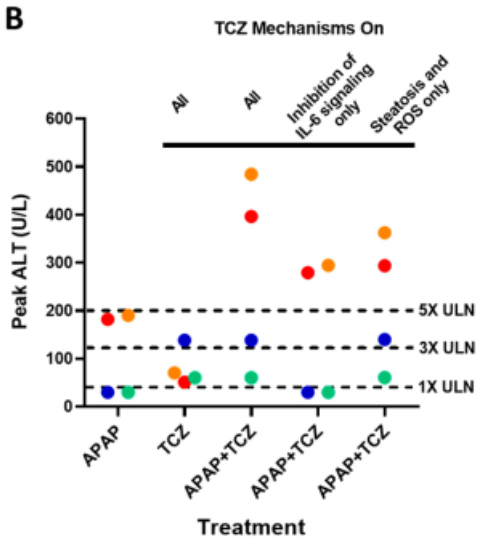


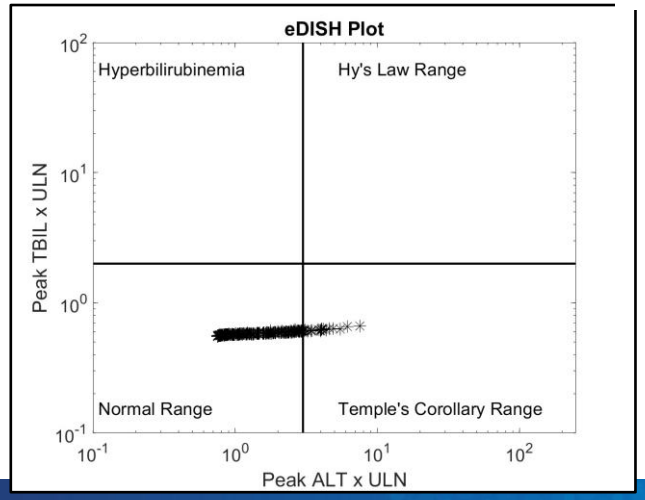
Beaudoin 2023, PMID 37298645

Combination of Known IL-6 Mechanistic Pathways and LAMPS-Informed Toxicity Pathways Reproduce TCZ DILI

- Initial BIOLOGXsym simulations conducted in a handful of virtual patients (N=4)
  - Baseline elevations in IL-6 levels, representative of RA patients
  - Mild DILI signals reproduced largely due to toxicity mechanisms (i.e., ROS)
  - Exploration indicated the potential for IL-6 pathway contributions under plausible conditions, e.g., APAP administration uncovers contribution of IL-6 on CYP3A4
- Population-level simulations (N=285) reproduce relatively frequent mild ALT elevations (1-3x ULN) and markedly lower frequency of clinically relevant ALT elevations (>3x ULN) qualitatively similar to published data







Beaudoin 2023, PMID 37298645

ALT >1x ULN: 153/285 (53.7%)
ALT > 3X ULN: 25/285 (8.8%)

Beaudoin 2026, QSPc (Leiden, The Netherlands)

Agenda

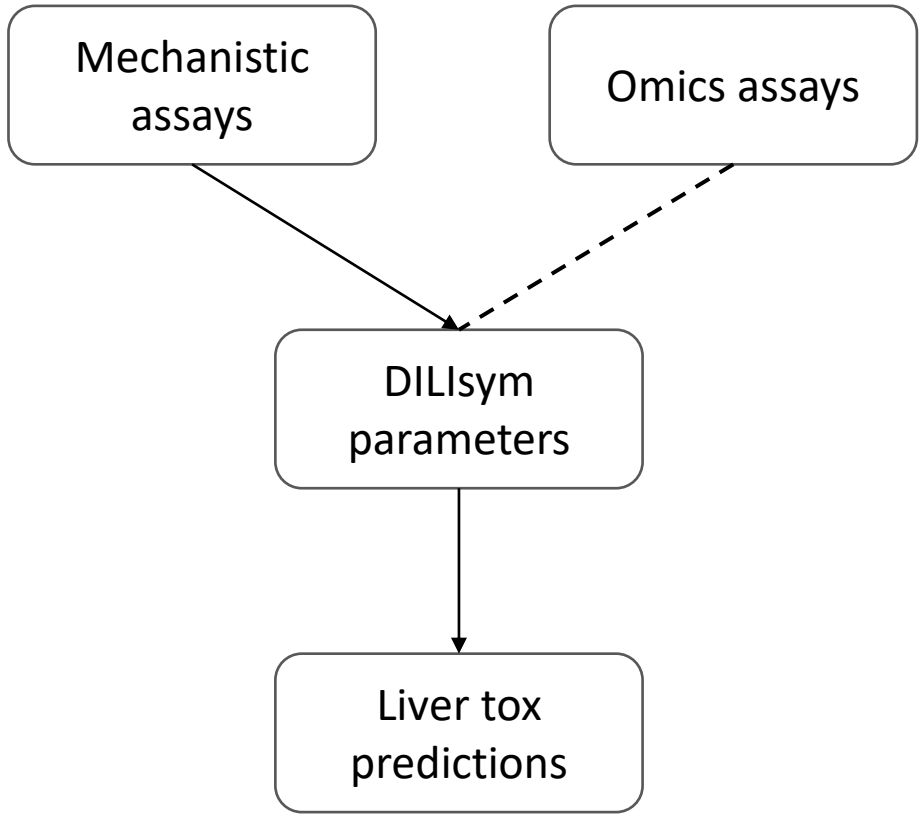
- Intro to QST and the DILIsym workflow
- Translation to biologics – BIOLOGXsym
- Novel biologic-induced toxicity mechanisms
- Next steps: siRNA drugs and other liver-on-a-chip systems

NAM UCC Work Could Expand Utility of DILIsym/BIOLOGXsym to New Input Modalities

- The NAM Use Case Collaborative (UCC) is a pre-competitive collaboration of various organizations to generate use cases that demonstrate end-to-end application and analysis of NAMs for an intended scientific purpose
  - BioIVT, Javelin Biotech, Precision Quantomics, Eurofins Discovery, Simulations Plus
- Current BIOLOGXsym work focused on mechanistic data derived from samples collected in the University of Pittsburgh liver acinus microphysiological system (LAMPs) as inputs
  - Demonstrated proof of concept with initial mAb compounds
  - Focused on a single not-well-adopted assay system
- NAMs UCC work focuses on predicting liver injury using Javelin/BioIVT liver on a chip system
  - Two siRNA therapeutics (fitusiran and inclisiran) used as initial compounds
  - Outputs include liver injury biomarkers and proteomics data
- Development of DILIsym compound models from NAM UCC data will lead to exploration of usage of novel data types as potential inputs into DILIsym

Proteomics as DILIsym/BIOLOGXsym Inputs – Challenges and Promise

- New therapeutic modalities (mAbs, ADCs, oligos, etc.) may need different assays to use as DILIsym inputs
  - Importance of considering more in vivo-like responses (i.e., target expression, multi-cellular interactions)
  - Liver-on-a-chip systems are becoming more common
  - Functional assays (e.g., effect on mitochondrial respiration) are hard to run on these systems
  - Logistic/financial limits on number of concentrations tested, replicates, and independent studies
- Omics data can be used for several purposes, not just for DILIsym
  - Avoids having to run an assay for DILIsym exclusively
- Converting proteomics data to mechanistic DILIsym inputs will require comparisons with known exemplars and lots of testing
  - NAM UCC project will provide fit-for-purpose data to test and holds the potential for future projects of similar or expanded utility



Acknowledgments

- James Beaudoin, Lara Clemens, Celeste Vallejo, Christina Battista, Francisco Huizar, Conner Sandefur, Vinal Lakhani, Michael Kelley, Scott Siler, Kyunghee Yang, Lisl Shoda
  - BIOLOGXsym development team, past and present
- Lans Taylor and the University of Pittsburgh LAMPS development team
- Members of the DILI-sim Initiative
- NIH Award R44TR003535
- Paul Watkins

Questions

This slide will stay visible during your Q&A. You may add your contact information, a web address, or other information that participants would need to follow-up on your talk.

