

# Career Path Design | The Future of a QSP/QST Modeling Scientist

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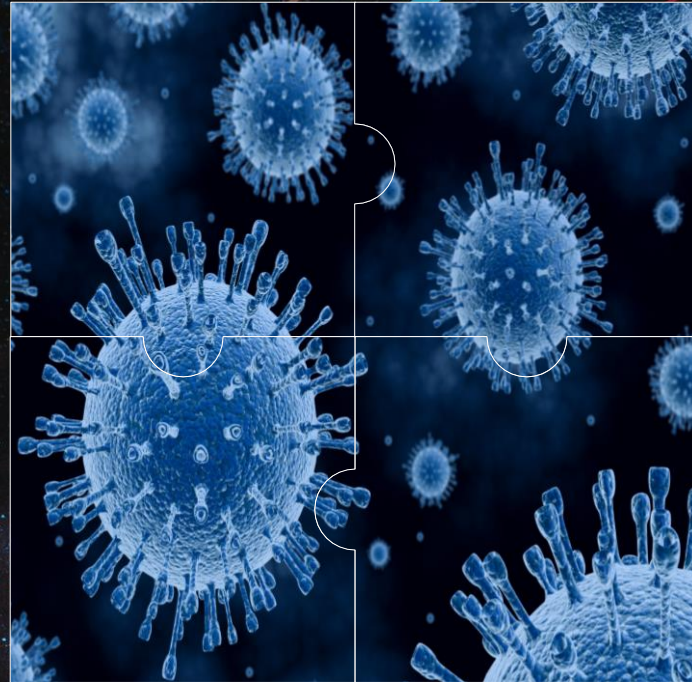
Please note: this presentation, including questions from the audience, is being recorded and may be made available.

# Executive Summary – QSP Career Path

- Quantitative systems pharmacology (QSP) modeling is a rewarding, fulfilling, and growing career opportunity to pursue
  - QSP (or quantitative systems toxicology, QST) is the process of using mathematics to represent biological systems, often in a diseased state, and probing disease progression + intervention scenarios
  - QSP modeling matters because it impacts key therapeutic development decisions or questions that are difficult to impact/inform with other methods
  - QSP modelers tend to come from a variety of scientific / technical training areas
  - Several action steps are available to migrate into QSP as a career path
  - The future of QSP is bright!
  - FAQ's will be discussed

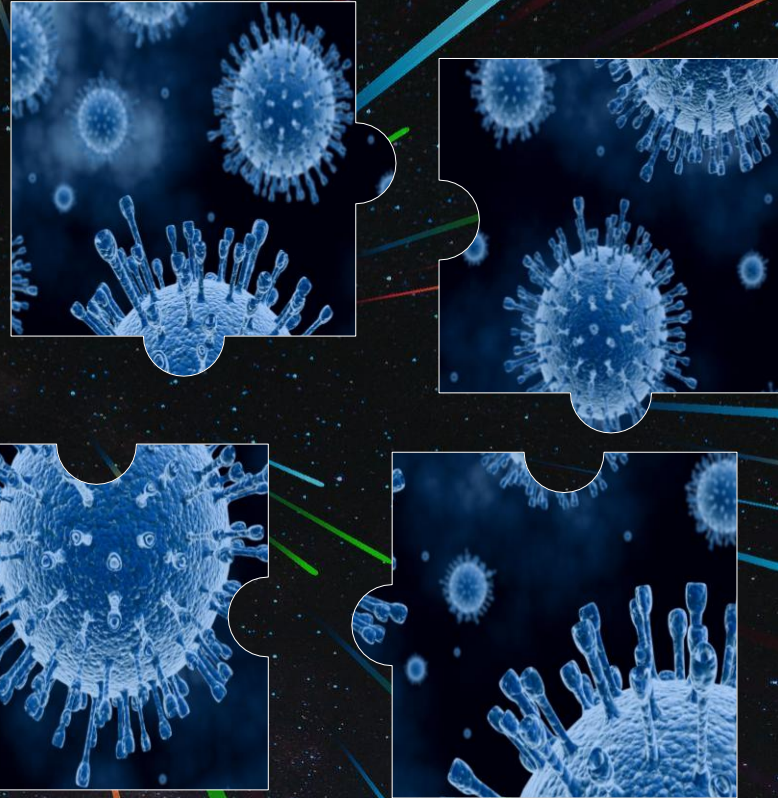
# Comparing QSP and PK-PD Models

- Traditional Pharmacokinetic / Pharmacodynamic (PK-PD) modeling uses statistical mathematics to infer relationships within clinical data (e.g. top down)
- Analogous to separating the pieces of a jigsaw puzzle to examine the separate shapes



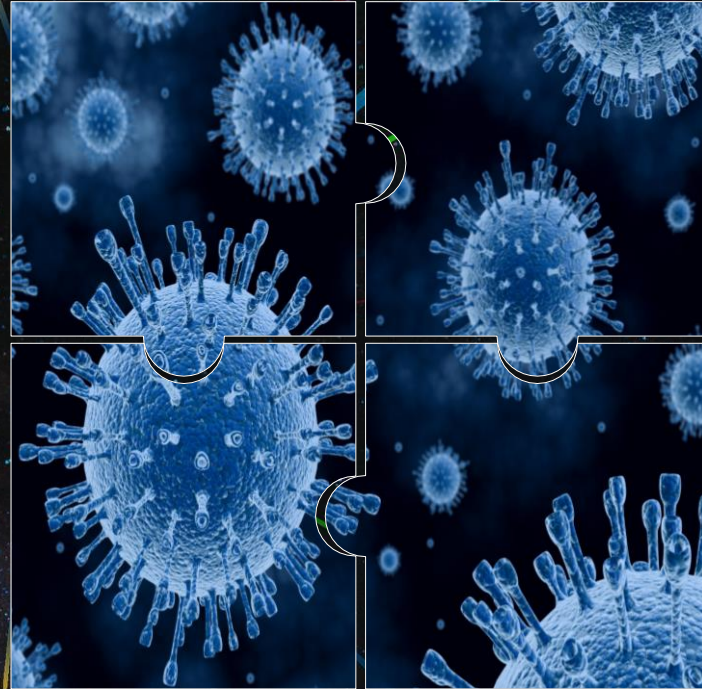
# Comparing QSP and PK-PD Models

- QSP modeling uses mathematics to represent relationships within data to form network of biochemical interactions (e.g. bottom up)
- Analogous to assembling the pieces of a jigsaw puzzle to examine the whole puzzle



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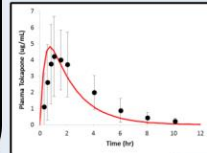


# QSP Modeling Predicts Efficacy and Safety of Drugs in Development

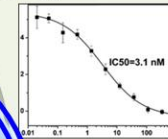


Predicted compound concentrations at site of target often require PBPK models

Exposure



Drug Effects



PD effects and Tox mechanisms are assessed in various ways

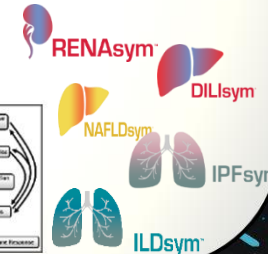
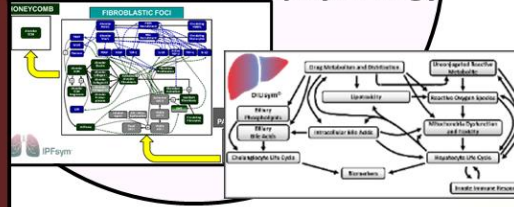
Tox Mechanisms



Efficacy and Tox

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

IPF and DILI Pathophysiology



# Why Does QSP Matter to the World?

- Provides confidence for safety decisions with biological rationale to support that confidence (e.g. Biohaven CGRP program)
- Allows for quantitative and less biased way to study mechanisms
- Addresses multi-factorial questions around patient behavior and confounding placebo effects
- Predicts acceptable or unacceptable efficacy levels prospectively for new therapies
- Provides framework for organizing complex data sets into clear conclusions
- FDA and other regulatory agencies are increasingly accepting and expecting QSP tools to be utilized when appropriate (e.g. around 60 FDA QSP submissions in 2020)



Application of the DILIsym<sup>®</sup> Quantitative Systems Toxicology drug-induced liver injury model to evaluate the carcinogenic hazard potential of acetaminophen

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# Typical Training Backgrounds for QSP Careers

- Engineers (e.g. biomedical, chemical, mechanical, etc.)
- Applied Mathematicians and Physicists
- Life Scientists (biologists, biochemists, etc.)
- Pharmaceutical Scientists (PhD with PharmD sometimes)
- Many others.....
- In general, QSP requires knowledge of complex biological systems with knowledge of mathematics
  - Starting place can be either side



# Migrating in the QSP Direction

1. Graduate research focused on mechanistic, mathematical problems in biology with emphasis on therapeutic development
2. Industrial internships (inquire, apply, ask).....
3. Commercial software access and training (e.g. SLP products like GastroPlus and DILIsym – University+ Program)
4. Surround yourself with current QSPers (technical meetings, societies, programming groups, regional chapters, etc.)
5. Homework on QSP literature and resources (papers, online webinars, posters, trainings, regulatory guidances, etc.)

# Daily Life of a QSP Modeler

- Extensive background research on diseases / biology (e.g. literature review, etc.)
- Model equation development, testing, and validation based on specified problem statement / context
- System / model usage to address specific application questions (e.g. execute simulations, organize and analyze resulting outputs, formulate conclusions, present internally and externally)
- Deliverable preparation (documents, slides, files, etc.)
- External communication via presentations and technical documents
- Stakeholder relationship management
- Personnel and contracts management
- Representation within a specific therapeutic development group
- Software / tool development / testing / training
- Organizational management

# How to Ensure Impact and Growth in Your QSP Career

- Be committed to both sides of the discipline (life sciences and quantitative sciences)
- Be collaborative (QSP community is small)
- Be a developer of therapeutics who uses QSP tools, not the other way around
- **Constantly assess tangible impact on decisions and programs and amass success stories where you played a role**
  - **Application is the focus, not necessarily the methods**

# The Future of QSP.....

- Central to decision making
- **QSP + AI = winning combination**
- More standardized as regulatory guidances are issued
- Computational power explosion will drive more meta-analyses
- QSP modelers will be industry leaders and decision makers



# Frequently Asked Questions

- What is a typical starting title / level for a new QSP scientist?
- What types of organizations can QSP scientists be employed by?
- What are the most important skills for a good career in QSP
  1. Succinctly conveying high impact information
  2. Knowing the goals / drivers
  3. Reading the room
- What types of technologies typically get used for QSP modeling?
- Is computer programming a required skill?
- Is QSP more applicable to small molecules or macromolecules?
- When is it too late to migrate into a QSP career?

 *SimulationsPlus*

# MIDD

Model Informed Drug Development + 2023

# Q&A

Questions & Answers