**TUESDAY MORNING WORKSHOP (8:30 am – 11:30 am)**

**B. (BIOMARKERS/PRE-CLINICAL/DISCOVERY) Statistical Approaches for Biomarker and Diagnostics**

**Organizer/Chair: Lin Li and Jennifer Schroeder, PharmaLex**

1. Discovering biomarker-treatment interactions with penalized regression

**Speaker: Abraham Apfel, BMS**

**TBA**

**2. Biomarkers to quantify renal decline in PKD patients**

Speaker: Douglas Landsittel, IU SPH

**TBA**

3. RAA:  The Development of a Robust and Automatic Annotation Procedure for Single-cell RNA Sequencing Data

**Speaker: Dongyan Yan, Eli Lilly**

**TBA**

**4. Trajectory Phenotyping for Medication for Opioid Use Disorder: Development of a Risk Stratification and Prediction Framework Using Urine Toxicology and EHR Data**

**Speaker: Albert Burgess-Hull, MATClinics**

**TBA**

**TUESDAY AFTERNOON WORKSHOP (1:30 pm – 4:30 pm)**

**B. (BIOMARKERS/PRE-CLINICAL/DISCOVERY) Experimental design and data analysis in discovery and developmental research**

**Organizer/Chair: Lin Li, PharmaLex; Hui-Rong Qian, Eli Lilly**

1. Whole-cage randomization for animal studies with unequal cage or group sizes

**Speakers: Steven Novick, Eli Lilly**

**TBA**

2. Multi-parameter optimization in antibody discovery

Speaker: Suntara Cahya Eli Lilly

**TBA**

3. Non-parametric Screening and Penalized Regression for Biomarker Discovery in NGS data with Time-To-Event Outcomes

Speaker: Lira Pi, PharmaLex

Recently, NGS data have become rapidly evolved in the manner of gigantic volume and data complexity. For drug-target discovery from NGS, although many data analysts utilize conventional FDR control methods for multiplicity adjustments, it has been well-known that the NGS data characteristics readily violate the assumptions of conventional methods and consequently produce low power. In this talk, we rather propose a series of machine learning methods, named BallXAL pipeline, by accounting for biomarker dependency and very weak true signals inherited in the NGS data. Our simulation studies proved the superior performance from the BallXAL pipeline for biomarker discovery, over other candidate methods such as Benjamini-Hochberg FDR control method.

4. Assay LOD determination using probit regression

Speaker: Shuguang Huang, Stat4ward

**TBA**

**WEDNESDAY MORNING WORKSHOP (8:30 am – 11:30 am)**

**B. (BIOMARKERS/PRE-CLINICAL/DISCOVERY) Statistical Approaches for Discovery and Preclinical Research**

**Organizers/Chairs: Lin Li and Erin Wagner, PharmaLex**

1. Bayesian Order Constrained Adaptive (BOCA) Design for Phase II Clinical Trials Evaluating Subgroup-Specific Treatment Effect

Speaker: Mu Shan, IU

The “one-size-fits-all” paradigm is inappropriate for phase II clinical trials evaluating biotherapies, which are often expected to have substantial heterogeneous treatment effects among different subgroups defined by biomarker. For these biotherapies, the objective of phase II clinical trials is often to evaluate subgroup-specific treatment effects. In this paper, we propose a simple yet efficient Bayesian adaptive phase II biomarker-guided design, referred to as the BOCA design, to detect the subgroup-specific treatment effects of biotherapies.

The BOCA design combines the features of the enrichment design and sequential design. It starts with a all-comers stage, and subsequently switches to an enrichment stage for either the marker-positive subgroup or marker-negative subgroup, depending on the interim analysis results. The go/no go enrichment criteria are determined by two posterior probabilities utilizing the inherent ordering constraint between two subgroups. We also extend the BOCA design to handle the missing biomarker situation. We conducted comprehensive computer simulation studies to investigate the operating characteristics of the BOCA design, and compared it with other existing and conventional designs.

The results shown that the BOCA design yielded the best overall performance in detecting the subgroup-specific treatment effects by jointly considering the efficiency and cost-effectiveness of the trials. The software for simulation and trial implementation are available for free download.

**2. Virtual Control Group for Preclinical Drug Safety Assessment**

**Speaker: Dean Li, Pfizer**

Virtual Control Group (VCG) is a concept proposed by the eTRANSAFE initiative in 2020 to enable the 3R (Replace, Reduce, and Refine) strategy. VCG aims to reduce the need of control animals in toxicological studies by matching test-article treated animals with random draws of historical control animals from a centralized repository, which was built by a group of pharmaceutical companies and contract research organizations. In this talk I will give my understanding and perspective of VCG and its future, regulatory considerations, as well as statistical caveats on the matching and randomization.

3. Dynamic Bayesian Causal Network Analysis

**Speaker: Ixavier Alonzo Higgins, Eli Lilly**

**TBA**