

## **BMPK Facility Data for Grants**

The Bioanalytical, Metabolomics, and Pharmacokinetics Shared Resource (BMPK) provides bioanalytical analysis, pharmacokinetic modeling, and consultation services to support discovery-based research and pre-clinical/clinical research and drug development. These services include study design and method consultation, formulation development and preparation, determination of proper sample storage conditions, sample analysis, data compilation, bioinformatics analysis, and PK/PD modeling. Collaboration between BMPK and investigators, faculty, and staff are conducted through iterative one-on-one meetings to prospectively plan and develop projects and grants, or to evaluate ongoing study conduct, milestones, and outcomes.

BMPK offers a wide variety of analytical methods as well as the capabilities to develop and validate new assays. BMPK provides highly sensitive measurements for numerous chemotherapeutic agents and their metabolites, along with endogenous compounds in a wide assortment of sample matrices (e.g., whole blood, plasma, serum, urine, cell pellets and media, xenografts, and a variety of tissue types from biodistribution studies) using innovative LC-MS and LC-MS/MS techniques. BMPK is also equipped to assess proteomic alterations in a number of sample matrices, using the innovative NGS-coupled high-throughput multiplex Olink assay.

Non-compartmental analysis (NCA) and PK/PD modeling and simulations are performed to gain insight into the mechanism of action and life cycle of cancer therapeutic agents as singular entities or in combination with other compounds, and to assess inter-individual and random variability within study populations. The information gained from past studies is used to optimize the design aspects of future research and clinical trials including dosing strategies and the selection of patient populations. BMPK serves as an essential component of CCSG's research efforts developing complementary collaborations between its bioanalytical and pharmacokinetic capabilities and the skill sets of other Shared Resources.

### **BMPK General Instrumentation:**

The BMPK laboratory is equipped with the following items: 3 biosafety cabinets; 3 exhaust fume hoods; an incubator; several microcentrifuges and table-top centrifuges; multiple refrigerators, -20 °C freezers, and -80 °C freezers with security alarm monitoring systems; two analytical balances; 96-well and tube nitrogen evaporators; pH meter; shakers, and rotators; a de-ionization (DI) water system, an in-house reverse osmosis (RO) water system; a yellow light room for handling of photosensitive compounds/materials; manual and electronic single-place and multi-channel pipets; solid phase extraction plate systems; a Bead Ruptor for tissue homogenizations; and water bath sonicators.

### **BMPK Analytical Instrumentation:**

- Olink Signature Q100: a benchtop system for protein biomarker analysis
- Sciex 7500 QTrap triple quadrupole (ESI-LC/MS/MS): contains a binary pump, a degasser, a vial/96-well plate autosampler, a column heater/cooler, and divert valve.
- Sciex 5500 QTrap triple quadrupole (ESI/APCI-LC/MS/MS): contains a binary pump, a degasser, a vial/96-well plate autosampler with rinse pump, a column heater/cooler, and divert valves.

- Sciex 5500 triple quadrupole (ESI/APCI-LC/MS/MS): contains a binary pump, a degasser, a vial/96-well plate autosampler with rinse pump, a column heater/cooler, a UV detector, and divert valves.
- Agilent 6545 QTOF (ESI-LC/MS/MS) high mass accuracy time of flight instrument with Agilent 1290 Infinity II Bio LC system able to operate at high pressures.
- Thermo Scientific TSQ Vantage triple quadrupole (ESI/APCI-LC/MS/MS): contains a binary pump, a degasser, a vial/96-well plate place autosampler, a column heater/cooler, and divert valves.
- Sciex API3000 triple quadrupole (ESI LC/MS/MS): contains a dual binary pumping system, a degasser, a vial/96-well plate place autosampler, a column heater, and divert valve.

### **BMPK Modeling and Statistical Software:**

- NONMEM: nonlinear mixed effect modeling software for population analysis to determine sources of variability in the PK and PD of drugs
- NextDose: posthoc estimations for busulfan therapeutic drug monitoring.
- R: open-source tool for statistical computing, data analysis, and graphics, widely used in data science, statistics, and research, offering powerful functions via packages for tasks such as descriptive statistics, data manipulation, and visualization, operating through scripts in a command-line interface, as well as non-compartmental and individual compartmental modeling PK and PK/PD analysis, data formatting, graphics and statistical summaries.