Septic Shock
Immunology and Inflammatory Disease

Endotoxins (lipopolysaccharide, LPS) are biologically active substances present in Gram-negative bacteria. Injection of purified LPS into experimental animals leads to the development of many biological activities that can lead to shock with lethal outcome. The toxic and other biological properties of LPS are caused indirectly through the action of endogenous mediators that are formed following interaction of LPS with cellular targets, macrophages occupying a key position in the development of endotoxin shock. Tumor necrosis factor alpha (TNF-alpha), a macrophage derived cytokine, is a primary mediator of the lethal action of endotoxin. Sensitivity to LPS is genetically determined, varying considerably among different species. The sensitivity of normal animals (mice) to endotoxin may be enhanced considerably under different experimental conditions that include treatment with live (infection) or killed Gram-negative and -positive bacteria.

Models Available:

• LPS Induced cytokine secretion in Mice
Validation Data: LPS Induced Cytokine Secretion in Mice

Study Protocol

1) Female Balb/c mice, 6wk at arrival, are acclimated 7 days.
2) Randomization 1 day prior experiment initiate.

LPS, 1 mg/kg/10ml by IP for each group (not include the blank group)

Dosing groups (10mice/group):
Gr1 Vehicle (20% HPbetaCD, PH6.8) PO
Gr2 Comp X, 20mpk PO
Gr3 Comp Y, 5mpk PO
Gr4 Comp Z- 10mpk PO
Gr5 Comp Z- 25mpk PO
Gr6 Comp Z- 50mpk PO
Gr7 Comp Z- 100mpk PO
Blank, n=2

1) Mice will be sacrificed by CO2 inhalation, Blood will be collected via cardiac puncture.
2) Measurements: (i) Serum TNFa by ELISA; (ii) Serum compound exposure by bioanalysis

Results

i. Compound Z suppresses TNF-a secretion in LPS induced cytokine secretion mice
BioDuro Pharmacology

The BioDuro Advantage

BioDuro’s pharmacology team has extensive drug discovery and development experience in the pharmaceutical industry enabling us to support fully integrated programs, including study design and data interpretation. Special expertise in metabolic and inflammatory diseases is coupled with a commitment to working with clients to develop customized models for rare diseases.

Our team has successfully collaborated with 9 of the top 20 large pharmaceutical companies and numerous small companies. The success of these collaborations is highlighted by the quality data provided that have informed key project decisions and regulatory filings. Beyond providing analysis, our senior team’s expertise allows for the development of a consulting relationship with client partners.

The Pharmacology Team

- Dr. Yong Qi, Directory of Pharmacology, has over 16 years of experience in leading and advancing drug discovery projects in metabolic and other disease areas at several pharmaceutical companies, including GlaxoSmithKline
- Group leader-level scientists with strong background and training in metabolic diseases
- A team of 20 well-trained bench scientists focused on in vitro and in vivo metabolic disease drug discovery services. They are skilled in different animal models/assays and excel in problem-solving and trouble-shooting

Services

- Translational research
- Biomarker discovery & development
- Compound efficacy evaluation
- Consultation

Therapeutic Focus

- CNS
- Inflammation and Immunology Disease
- Metabolic Disease