Rheumatoid arthritis (RA) is a chronic debilitating autoimmune disorder characterized by synovitis that leads to cartilage and bone erosion by invading fibrovascular tissue. Mouse and Rat models of RA recapitulate many features of the human disease. Despite the availability of medicines that are highly effective in many patient populations, autoimmune diseases (including RA) remain an area of active biomedical research, and consequently mouse models of RA are still extensively used for mechanistic studies and validation of therapeutic targets.

Models Available:

- Collagen-Induced Arthritis (CIA) in DBA/1 Mice
- Collagen-induced arthritis (CIA) in Lewis rats
- Adjuvant-Induced Arthritis AIA in Lewis Rats
- G6PI-Induced Arthritis in DBA/1 Mice
Validation Data: Collagen-Induced Arthritis (CIA) in DBA/1 Mice

Study Protocol

Results

i. Body weight, Incidence of CIA and Disease Score

Two-way ANOVA, Bonferroni’s Posttests, *p<0.05, **p<0.01, ***p<0.001 vs. Vehicle
ii. Histology

One-way ANOVA, Bonferroni’s Posttests, **p<0.01 vs. Vehicle
iii. Serum cytokines

One-way ANOVA, Bonferroni’s Posttests, *p<0.05, **p<0.01, ***p<0.001 vs. Vehicle
**Validation Data:** Collagen-Induced Arthritis (CIA) in Lewis rats

**Study Protocol**

- Female Lewis rats 6-8 wk at arrival
- Acclimated for 7 days
- 48 rats are randomized to 6 groups

<table>
<thead>
<tr>
<th>Days</th>
<th>Groups (8 rats/group):</th>
</tr>
</thead>
<tbody>
<tr>
<td>-7</td>
<td>Gr1 Vehicle (5% HPMC) PO qd</td>
</tr>
<tr>
<td>-1</td>
<td>Gr2 Dex, 0.1 mpk PO qd</td>
</tr>
<tr>
<td>0</td>
<td>Gr3 Ibuprofen, 100 mpk PO qd</td>
</tr>
<tr>
<td>7</td>
<td>Gr4 High dose, 90 mpk PO qd</td>
</tr>
<tr>
<td>27</td>
<td>Gr5 Mid dose, 30 mpk PO qd</td>
</tr>
<tr>
<td></td>
<td>Gr6 Low dose, 10 mpk PO qd</td>
</tr>
</tbody>
</table>

1. Bovine CII in Acetic acid (100 uM, 5mg/ml)
2. Incomplete Freund’s adjuvant
3. Emulsify Bovine CII solution in an equal volume of the CFA with homogenizer (~60 min)
4. Anesthetize the rats with isoflurane
5. 100 μL emulsion ID at the base of tail

*Body weight, Clinical Score, Incidence, Paw volume: All rats will be recorded twice a week from Day 7 to Day 27*

- 1) Euthanized via CO2, Hind paws will be fixed in 10% NBF
- 2) Measurement: T-blue stain

**Results**

i. **Body weight**

![Body weight graph](image)
Rheumatoid Arthritis

ii. Incidence of CIA

![Incidence of Disease Graph]

iii. Incidence of CIA

![Clinical Score Graph]
iv. Histology

v. Histology scores:

a) Filtration of cells

One-way ANOVA, Bonferroni’s Posttests, *p<0.05, **p<0.01 vs. Vehicle
b) Pannus severities

Ono-way ANOVA, Bonferroni’s Posttests, **p<0.01 vs. Vehicle

![Pannus severity graph]

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c) Cartilage lesion severities

One-way ANOVA, Bonferroni’s Posttests, *p<0.05, **p<0.01 vs. Vehicle

![Cartilage lesion severity graph]
Validation Data: Adjuvant-Induced Arthritis (AIA) in Lewis rats

Study Protocol

Groups (10 rats/group):
- Gr1 Vehicle (5% HPMC) PO BID
- Gr2 Cpd A, 3 mpk PO BID
- Gr3 Cpd A, 10 mpk PO BID
- Gr4 Cpd A, 30 mpk PO BID
- Gr5 CSA, 5 mpk PO BID
- Gr6 Normal (5 rats/group)

Female Lewis rat
140-160g at arrival
Acclimated for 7 days

55 rats randomized to 6 groups

1) M. tuberculosis suspension in Paraffin oil (10 mg/ml)
2) Anesthetize the rats with isoflurane
3) 100 µL SC injection into the left foot pad, Control animals, 100 µL of Paraffin oil

Body weight, Clinical Score, Incidence, Paw volume: Recorded every two days from Day 0 to Day 18

1) Serum compound exposure: After last dose, three animals from each group for plasma PK (0h, 2h, 4h, 6h, 12h). (Orbital)
2) Histopathology: sacrificed by CO2 inhalation, Five animals from each group. Hind paws will be fixed in 10% NBF
3) Measurements: Serum IL-17A and IL-6 by ELISA
Results

i. Body weight, Incidence of CIA and Disease score

Two-way ANOVA, Bonferroni’s Posttests, **p<0.01, ***p<0.001 vs. Vehicle

ii. Paw volume

Two-way ANOVA, Bonferroni’s Posttests, ***p<0.001 vs. Vehicle
iii. Paw volume

One-way ANOVA, Bonferroni’s Posttests, *p<0.05, **p<0.01, ***p<0.001 vs. Vehicle
Validation Data: G6PI- induced arthritis in DBA/1 mice

Study Protocol

Male DBA/1 mice
18-20g at arrival
Acclimated for 7 days

90 mice randomized to 6 groups

Days -7 -1 0 7 17

Treatment (15 mice/group):
Gr1 Vehicle (5% HPMC) PO BID
Gr2 Cpd A, 1 mpk PO BID
Gr3 Cpd A, 3 mpk PO BID
Gr4 Cpd A, 10 mpk PO BID
Gr5 Cpd A, 30 mpk PO BID
Gr6 Dex, 1 mpk PO BID

Body weight, Paw thickness :
Recorded every two days from Day 6 to Day 17

Serum compound exposure : After last dose, three animals from each group for plasma PK (0h, 0.25h, 0.5, 1h, 3h, 7h, 12h).
(Orbital)

1) Glucose-6-phosphate isomerase (hG6PI) protein (G6PI) in PBS (6mg/ml)
2) Complete Freund’s adjuvant(CFA)(4 mg/ml)
3) Emulsify G6PI solution in an equal volume of the CFA with Homogenizer (~60 min) *
4) Anesthetize the mice with Isoflurane
5) 100 µL emulsion, ID at the base of the tail

* A stable emulsion should not disperse when a drop is placed on an aqueous surface.

Results

i. Body weight and Paw thickness

Two-way ANOVA, Bonferroni’s Posttests, *p<0.05, **p<0.01, ***p<0.001 vs. Vehicle
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