Citric Acid Induced Cough Model in Guinea Pig

**Selection of Cough Animals**
1. Exposure to 17.5% citric acid aerosol for 5 min
2. >= 10 coughs

**Dosing**
- Dextromethorphan hydrobromide 60mpk, PO
- Vehicle (PBS), PO
- Cpd X 30mpk, PO

**Cough study**
1. Re-exposure to 17.5% citric acid aerosol for 5 min
2. a. Latency to cough (sec)
   b. Counts of cough (5min)

**Study outline**

Days: -5 ~ -7 day

Male Guinea Pigs,
Body weight 140-180g
7 days acclimation

Groups (8/group):
- Vehicle (PBS), PO
- Dextromethorphan hydrobromide 60mpk, PO
- Cpd X 30mpk, PO
Citric Acid Induced Cough Model in Guinea Pig

**Number of Coughs**

<table>
<thead>
<tr>
<th>Vehicle</th>
<th>Dextromethorphan hydrobromide</th>
<th>Cpd X</th>
</tr>
</thead>
<tbody>
<tr>
<td>Counts (5 min)</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>Latency (Sec)</td>
<td>* -42.6%</td>
<td>* -39.1%</td>
</tr>
</tbody>
</table>

**Latency (Sec)**

- Vehicle: 30.9%
- Dextromethorphan hydrobromide: 30.9%
- Cpd X: 59.6%
Study outline

1) Female Balb/c mice, 7-8wk at arrival, acclimated for 7 days.
2) Randomization: 1 day prior experiment initiate
   1. PBS/Veh (20%HPβCD), PO (n=10)
   2. OVA/Veh (20%HPβCD), PO (n=10)
   3. OVA/Dex – 1 mpk, SC (n=10)
   4. OVA/CpdX – 0.2 mpk, PO (n=10)
   5. OVA/ CpdX – 1 mpk, PO (n=10)
   6. OVA/ CpdX – 5 mpk, PO (n=10)
   7. OVA/ CpdX – 20 mpk, PO (n=10)
   8. OVA/ CpdX – 50 mpk, PO (n=10)

Challenge:
5% OVA aerosol, 20 min

Sensitization:
10 μg OVA/Alum i.p.

Termination:
24 h after final challenge with 5% OVA, animal will be anesthetized.

Blood and BAL will be collected:
- BAL total and differential cell count,
- BAL cytokines (IL-5)
- Serum IgE assay

Statistics:
- One-way ANOVA, Dunnett’s Multiple comparison test
- Data are Mean ± SEM
- * p<0.05, **p<0.01, ***p<0.001 vs. Ova
OVA Induced Allergic Asthma Mice

Inflammatory Cells of BALF

Total Cells of BALF

IL-5 of BALF

Blood IgE

- One-way ANOVA, Dunnett’s Multiple comparison test
- Data are Mean ± SEM
- * p<0.05, **p<0.01, ***p<0.001 vs. Ova
Airway resistance

*P<0.05, **P<0.01, ***P<0.001, vs G1, Two Way ANOVA, Bonferroni posttests tests