**Male C57/BL6J mice maintained on high fat diet (45% energy as fat, D12451, Research Diets Inc.) for 3-4 months to induce obesity (60% kcal fat diet is also available)**

**Key features of model**
- Development of obesity depends on multiple genes and more closely resembles common human obesity than genetic models.
- Animals become weight-stable.
- Marked visceral adiposity (30-35%).
- Insulin-resistance.

**Advantages over DIO rats**
- Food given as a single source therefore studies easy to perform.
- Cheaper.
- Less compound required.
- Body composition can be determined throughout studies using DEXA.

**Bespoke study design**
- Acute, sub-chronic or chronic drug administration by a variety of routes.
- Body weight and food and water intake measurements.

**Optional additional studies include:**
- Glucose tolerance tests to assess effects of drugs on glycaemic control.
- Blood-sampling for PK or to determine levels of comorbid risk factors/other biomarkers.
- Body composition analysis to confirm weight-loss is due to selective fat loss.

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**RenaSci: Mouse Model of Dietary-induced Obesity**

**Weight-loss Produced by Centrally- and Peripherally-acting Drugs**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Body weight</th>
<th>Adiposity</th>
<th>Insulin resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Topiramate/phentermine</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Rimonabant</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Sibutramine</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Orlistat</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Liraglutide</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Rosiglitazone</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
</tr>
</tbody>
</table>

**Useful Screen for Antiobesity and Antidiabetic Potential**

**OGTT: AUC (0-60 min)**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Vehicle 3 ml/kg po</th>
<th>Rosiglitazone 3 mg/kg po</th>
<th>Rosiglitazone 10 mg/kg po</th>
<th>Topiramate 5 mg/kg po</th>
<th>Rimonabant 5 mg/kg po</th>
<th>Rimonabant 10 mg/kg po</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Drug</strong></td>
<td><em>p&lt;0.05</em>*</td>
<td><strong>p&lt;0.01</strong></td>
<td>*<strong>p&lt;0.001</strong></td>
<td><strong>p&lt;0.01</strong></td>
<td><strong>p&lt;0.01</strong></td>
<td><strong>p&lt;0.01</strong></td>
</tr>
</tbody>
</table>

Blood samples taken at baseline (0 min) following an overnight fast and 15, 30 and 60 min post-glucose (2 g/kg po). 4 weeks of treatment. In all figures n=8-10. **p<0.05, ***p<0.001. **

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