Rodent Models of Cardiovascular Disease

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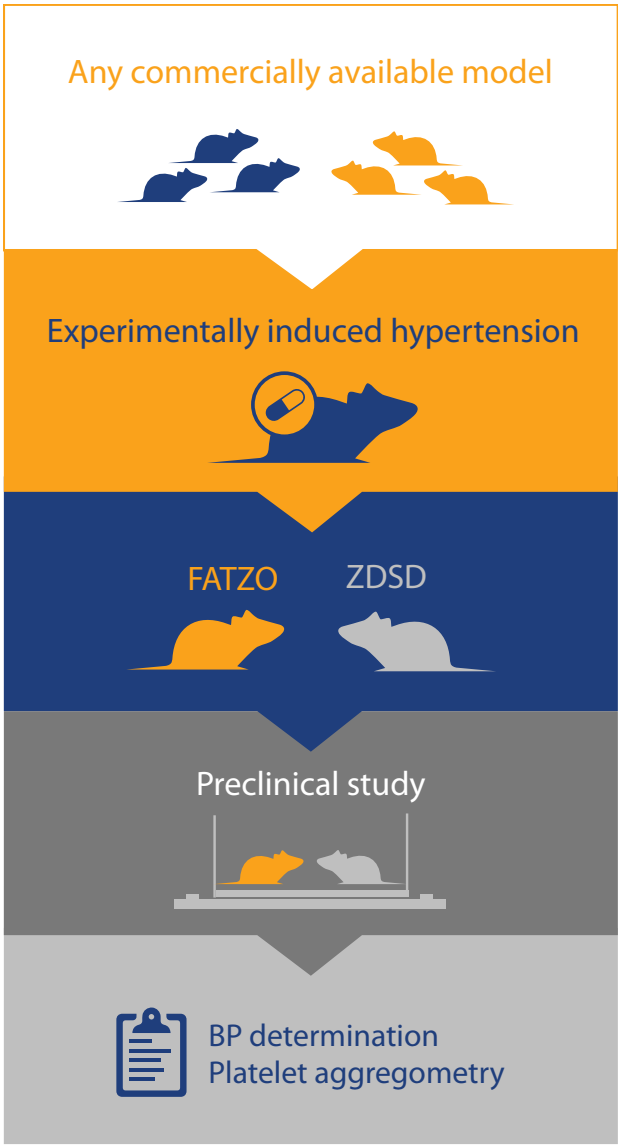
A collection of conventional and highly translatable rodent models for CVD research

Discover how our wide-ranging collection of rodent models, combined with key blood pressure and platelet aggregometry technologies, can progress your cardiovascular disease research.

Rodent models are a key first stage in *in vivo* preclinical translational studies; however, for cardiovascular disease (CVD) research this is complicated by a lack of hypertension in some commonly used models. Appropriate translational models featuring high blood pressure are required for CVD drug and antihypertensive development.

A comprehensive rodent CVD research platform to rapidly progress preclinical drug development:

- Use any commercially available rat or mouse model for historical data consistency.
- Experimentally induced hypertensive models.
- Proprietary, highly translational models of dysmetabolism - the polygenic FATZO mouse and ZDSD rat, with ZDSD naturally developing hypertension.
- Monitor key CVD endpoints of blood pressure and platelet aggregometry.
- Advanced models for abdominal aortic aneurysm and atherosclerosis studies.



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Rodent Models of Cardiovascular Disease Key Facts

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Our comprehensive rodent CVD research platform is used to progress novel agents treating core CVD components such as hypertension:

- Via monitoring of two key endpoints in CVD research:
  - Blood pressure determination using the non-invasive tail cuff method, as well as continuous telemetry monitoring, with readouts such as mean arterial pressure, systolic and diastolic pressure, and heart rate.
  - Platelet aggregometry, via a range of agonists e.g. collagen, thrombin, serotonin, or arachidonic acid.
- In highly translatable polygenic models of dysmetabolism – the FATZO mouse and ZDSD rat, with the ZDSD model naturally developing hypertension on a normal chow diet.
- As well as any conventional and induced CVD models for consistency with historical research:
  - Any commercially available rat or mouse model.
  - Experimentally induced hypertension models such as uni-nephrectomized Sprague-Dawley Rats receiving aldosterone and salt in their drinking water.
- With cardiovascular models also available for advanced CVD studies:
  - For investigation of abdominal aortic aneurysm in mice (both angiotensin II and elastase induced).
  - To study rodent atherosclerosis via an ApoE knockout mouse fed a high cholesterol diet.

Blood Pressure Monitoring

CrownBio provides two approaches for BP monitoring. For a rapid review of rat or mouse BP the tail-cuff method can be performed, monitoring BP and heart rate (HR) non-invasively in up to eight animals at any one time. For a more high definition BP evaluation, radio telemetry is also available. Our system is fully enclosed within the test animal, with the monitor usually implanted in the abdominal aorta and the battery localized in the abdominal cavity. The animal cage is placed on a receiver, allowing continuous BP measurement as required (experiments can be performed over several months if needed). Experimental readouts include mean arterial pressure (MAP), systolic and diastolic pressures, and HR.

Example telemetry data is shown in **Figure 1** and **Figure 2. Figure 1** shows hourly and daily MAP telemetry data in uni-nephrectomized male Sprague-Dawley rats with induced hypertension. Eplerenone (a mineralocorticoid receptor antagonist) was used to validate the model and, following administration, a dose-dependent reduction in MAP was observed by continuous telemetry over 15 days. **Figure 2** displays example data for the FATZO Type 2 diabetic mouse model. The FATZO mouse has increased MAP compared to control, but also has lower activity levels, specifically during the active phase of 6pm to 6am.

Figure 1: Eplerenone Reduces BP in Uni-Nephrectomized Male, Sprague-Dawley Rats as Monitored by Continuous Telemetry
Hourly and daily telemetric averages. Uni-nephrectomized male, Sprague-Dawley rats receiving aldosterone via Alzet minipump and salt in the drinking water.

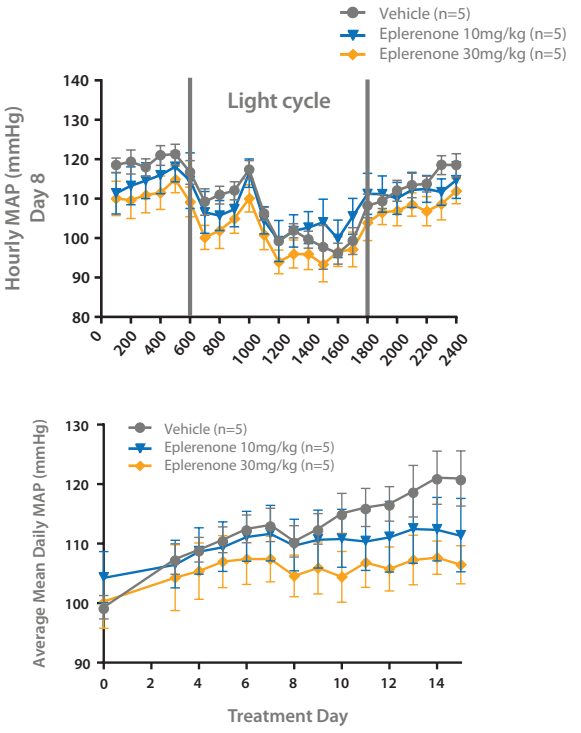

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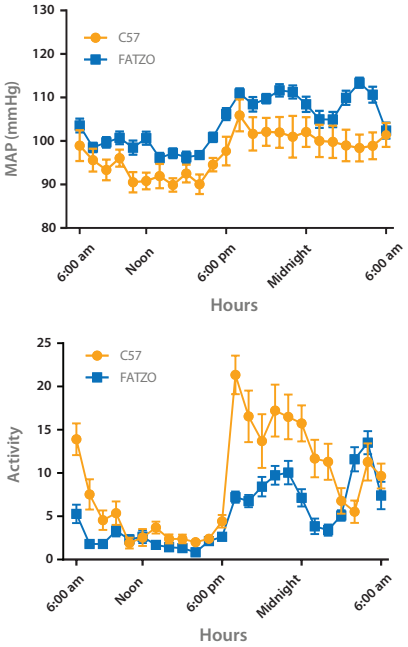
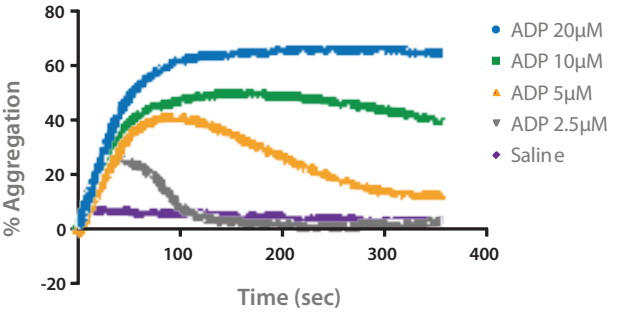
Figure 2: Increased Blood Pressure and Reduced Activity in the FATZO Mouse



Platelet Aggregometry

CrownBio also provides platelet aggregometry assessment, to evaluate the effects of novel compounds on platelet function. **Figure 3** shows example data using the known aggregation agonist ADP, with a concentration-dependent increase in aggregation observed following administration to rat platelets. We can provide a range of agonists to meet your research needs (including collagen, thrombin, serotonin, or arachidonic acid). Novel agents can be added to the assay to evaluate the level with which they inhibit platelet aggregation.

Figure 3: ADP Induces Concentration-Dependent Platelet Aggregation



Summary

CrownBio provides both non-invasive tail-cuff and telemetry methods for evaluating BP and novel antihypertensive agents, allowing rapid or prolonged, continuous monitoring as required. We also provide platelet aggregometry evaluation. These procedures can be performed in any commercially available rat or mouse model (allowing consistency with historical data) and also in models with experimentally induced hypertension. Our assays are validated with positive controls for lowering BP and platelet aggregation.

We also provide these procedures in more human disease translatable models including the FATZO mouse and ZDSD rat. These polygenic models of dysmetabolism naturally develop CVD on a normal diet and without leptin/leptin receptor mutations, closely mimicking human dysmetabolic syndrome and providing more translatable research models. At CrownBio we are committed to furthering research in the CVD field and are currently developing advanced models to enable the study of heart failure and thrombosis.