CrownBio
CONNECTING SCIENCE TO PATIENTS

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# Rodent Models of Cardiovascular Disease

## Explore CrownBio's Collection of Conventional and Highly Translatable Rodent Models for CVD Research

Cardiovascular disease (CVD) is a group of disorders affecting the heart and blood vessels including coronary heart disease, peripheral arterial disease, stroke, and aortic disease. Risk factors for CVD include hypertension, smoking, high blood cholesterol, diabetes, and being overweight/obesity[1]. CVD has become a major public health problem worldwide, and is the number one cause of death globally, with the World Health Organization estimating that 17.5 million people died from CVD in 2012 (31% of all global deaths)[2].

Many deaths caused by CVD are premature, and could be prevented by lifestyle changes such as regular exercise, healthy eating, and stopping smoking. In addition to these changes, drug treatments for certain elements of CVD may be necessary e.g. for hypertension to reduce cardiovascular risk and to prevent both heart attack and stroke[2]. Appropriate preclinical technologies and models are therefore required for the evaluation of treatments for CVD; however, this is complicated by a lack of hypertension in some currently used research models e.g. the ZF rat.

### CrownBio Cardiovascular Technologies and Resources

Two key procedures we provide for cardiovascular research are blood pressure (BP) monitoring (via the non-invasive tail-cuff method and continuous telemetry) and platelet aggregometry. These can be performed in any commercially available rat or mouse model, allowing consistency with historical data where required. We can also perform these procedures in models with experimentally induced hypertension such as uni-nephrectomized Sprague-Dawley Rats receiving aldosterone and salt in their drinking water. As the salt level is increased, stress on the remaining kidney also increases, leading to the animal developing hypertension and renal injury (detailed in our Rodent Models of Renal Disease Factsheet).

We also provide highly translatable models of cardiovascular disease including the FATZO mouse and ZDSD rat. These are polygenic models of dysmetabolism without leptin/leptin receptor mutations which closely mimic the human condition, developing obesity, metabolic syndrome, and diabetes. The ZDSD rat naturally develops high blood pressure on a normal chow diet, providing a suitable model for CVD research and antihypertensive evaluation. ZDSD rats present elevated biomarkers for an activated renin–angiotensin–aldosterone system (RAAS), endothelial dysfunction, aberrant vasoconstriction, and a prediabetic hypertensive state which has been confirmed via the tail-cuff method and telemetry. Factsheets are available on both the FATZO mouse and ZDSD rat detailing their full dysmetabolic characteristics.

CrownBio also provides advanced cardiovascular models to investigate abdominal aortic aneurysm in mice (both angiotensin II and elastase induced), and to perform rodent atherosclerosis studies using the 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.

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**Figure 1: Eplerenone Reduces BP in Uni-Nephrectomized Male, Sprague-Dawley Rats as Monitored by Continuous Telemetry**

Hourly telemetric averages and daily telemetric averages. Uni-nephrectomized male, Sprague-Dawley Rats receiving aldosterone via Alzet minipump and salt in the drinking water.

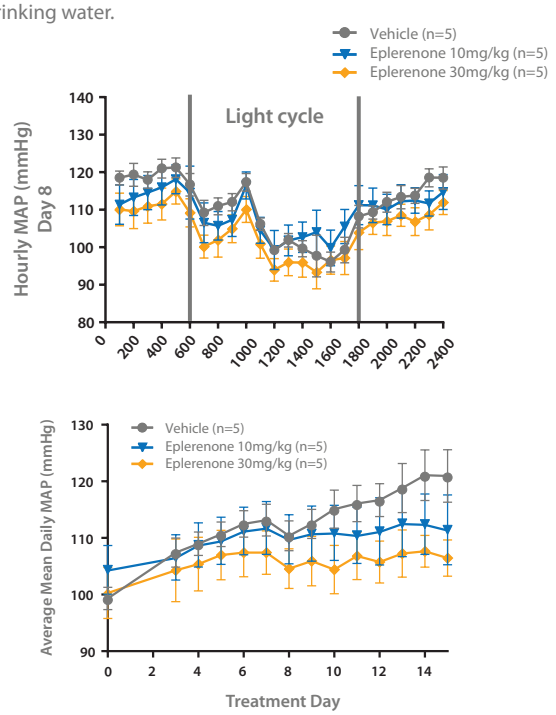
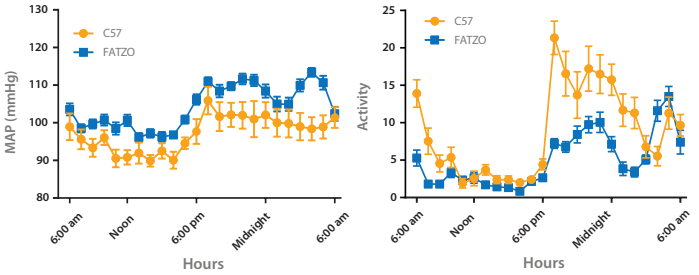


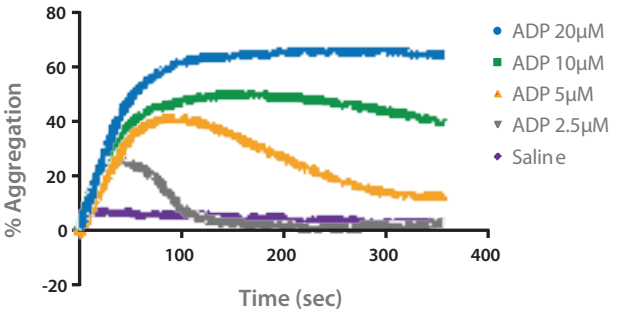

**Figure 2: Increased Blood Pressure and Reduced Activity in the FATZO Mouse**




## 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

CVD is a group of disorders affecting the heart and blood vessels including coronary heart disease, peripheral arterial disease, stroke, and aortic disease. CVD is the leading cause of death worldwide, and is a major public health problem. Appropriate preclinical technologies and models are required for the evaluation of treatments for CVD; however, this is complicated by a lack of hypertension in some currently used research models e.g. the ZF rat.

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.

Discover the benefits of working with CrownBio to successfully translate your CVD research into the clinic. Contact us today at **busdev@crownbio.com** for a free consultation about selecting the technologies and models that meet your project needs.

## References

[1]NHS website. Cardiovascular disease, Overview. http://www.nhs.uk/conditions/cardiovascular-disease/Pages/Introduction.aspx Accessed 05 May 2015.
[2]World Health Organization website. Cardiovascular diseases (CVDs) Fact sheet No317, updated January 2015. http://www.who.int/mediacentre/factsheets/fs317/en/ Accessed 05 May 2016.