

# METABOLIC EXPLORATION

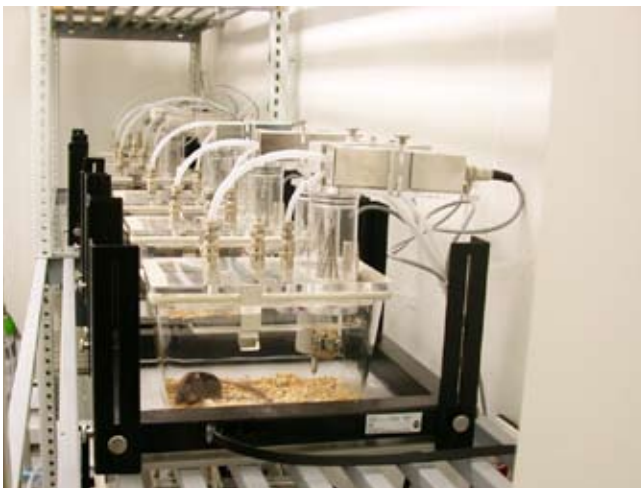
## PRESENTATION

Metabolic dysfunctions are involved in some of the most common disease conditions occurring in developed societies, such as obesity, insulin resistance, type 2 diabetes, hyperlipidemia and atherosclerosis.

Characterization of metabolic dysfunction in mice is now of utmost importance for basic and clinical research.

Various tests are available to address the challenge of accurately detecting and assessing the often subtle changes in metabolic function in mice. The test battery adapted to the mouse includes analysis of food and water consumption, body weight and body composition, measurement of energy expenditure, evaluation of thermogenesis, exercise test and evaluation of glucose tolerance and insulin sensitivity. These tests are complemented by a wide range of blood analysis (glucose and lipid measurement, endocrine parameters...).

Alternatively, one or more specific tests can be performed individually or several tests can be bundled in a screening package to be used both for phenotyping genetically modified mice and to screen potential therapeutics in vivo in mice.

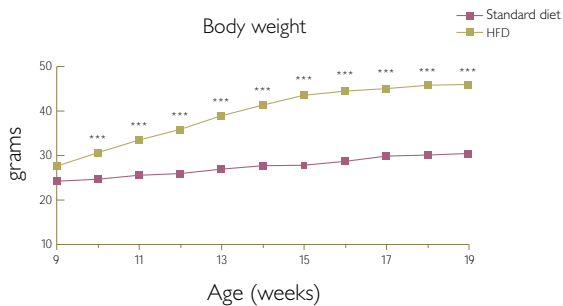




## 1. FOOD CONSUMPTION AND BODY WEIGHT

Ad libitum food consumption is monitored by weighing the food in the cage once a week for a defined period of time. Concomitantly body weight is recorded by weighing the mice once a week. More precise measurement can be recorded in metabolic cage or in Labmaster system.

Body weight evolution in mice fed with standard diet and with high fat/high sucrose diet (HFD)

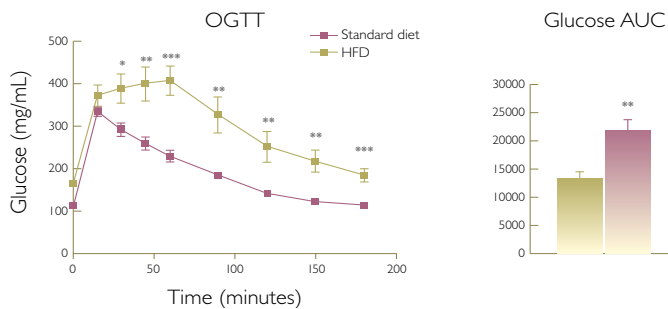


## 2. GLUCOSE TOLERANCE AND INSULIN SENSITIVITY TEST

### Intraperitoneal glucose tolerance test (IPGTT) or oral glucose tolerance test (OGTT)

The glucose tolerance test measures the clearance of an intraperitoneally or orally injected glucose load from the body. Animals are fasted for approximately 16 hours, a solution of glucose is administered by intra-peritoneal (IP) injection or by oral gavage and blood glucose is measured at different time points for 3 hours.

Oral glucose tolerance test in C57Bl/6J mice fed with standard diet and with high fat/high sucrose diet (HFD) AUC: area under the curve.



### Insulin sensitivity test (IPIST)

The insulin tolerance test measures glucose levels subsequent to a standardized insulin load. It gives an estimate of the insulin sensitivity of the animals.

Animals are fasted for approximately 16 hours, a solution of insulin is administered intra-peritoneally (IP) and blood glucose is measured at different time points during 90 minutes.

### Euglycemic clamps

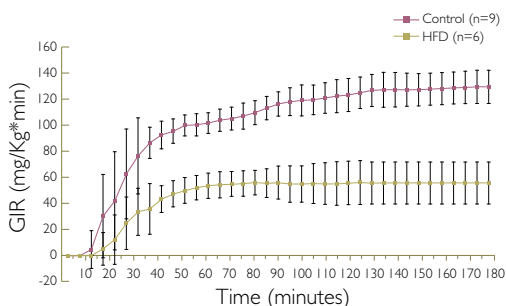
Euglycemic clamps are performed to evaluate differences in the time course of insulin action.

A catheter is placed in the femoral vein under anaesthesia 2-3 days in advance of the study.

The clamps are performed in awake, unanaesthetized mice after a 5 hours fasting.

Euglycemic clamp in C57Bl/6J mice fed with standard diet and with high fat/high sucrose diet (HFD)

Glucose infusion rate during Euglycemic clamp



### 3. ENERGY EXPENDITURE

Energy expenditure is evaluated through indirect calorimetry with different apparatus:

#### Oxymax

The system allows to measure daily (18 to 24 hours measurement) oxygen consumption, carbon dioxide production and to calculate respiratory exchange ratio (RER). In addition total and ambulatory activities are recorded in the Oxymax cages.

#### Labmaster (TSE)

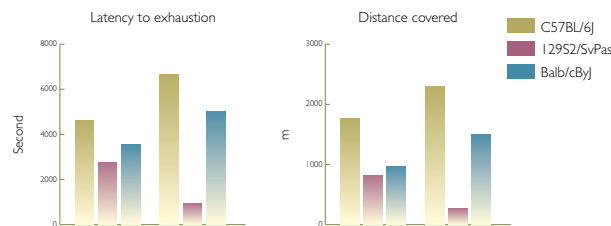
The system allows to measure daily (18 to 24 hours measurement) oxygen consumption, carbon dioxide production and to calculate respiratory exchange ratio (RER). Total and ambulatory activities are recorded in the Labmaster cages. Food intake and water consumption is also measured in these cages.

### 4. EXERCISE TEST

#### Exhausting exercise test

Exercise performance is assessed by treadmill exercise. Treadmill system consists of a belt, which is enclosed in a plexiglass chamber, with a stimulus device consisting of a metal shock grid attached to the rear of the belt. The speed and slope of the belt are electronically adjusted.

#### Exercise test in different mice strains



### 5. COLD TEST

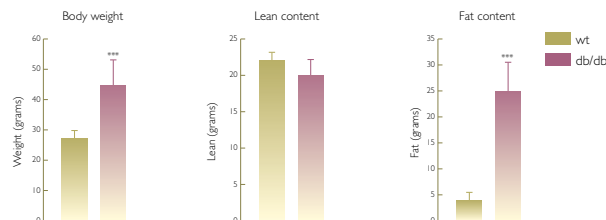
The cold test allows exploring adaptative thermogenesis that is a key component of energy balance.

### 6. BODY LEAN AND FAT CONTENT

#### Dexascan analysis

Body lean and fat content are recorded on anaesthetized mice by Dexascan analysis. At the same time bone mineral density and bone mineral content are also recorded

#### Evaluation of lean and fat content by Dexascan analysis in db/db mice



#### Quantitative Nuclear Magnetic Resonance (qNMR)

qNMR provides a very precise, accurate, fast and easy-to-use method for determining fat, lean tissues and free body fluids of mice without requiring anesthesia. The analysis is performed by a Minispec analyser:

#### qNMR analysis of C57Bl/6j mice fed with standard chow diet and with high fat/high sucrose diet (HFD)

