Non-Human Primate Models of Obesity

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Increase your chances of success in the clinic by using our translatable non-human primate (NHP) models of obesity in your dysmetabolism research

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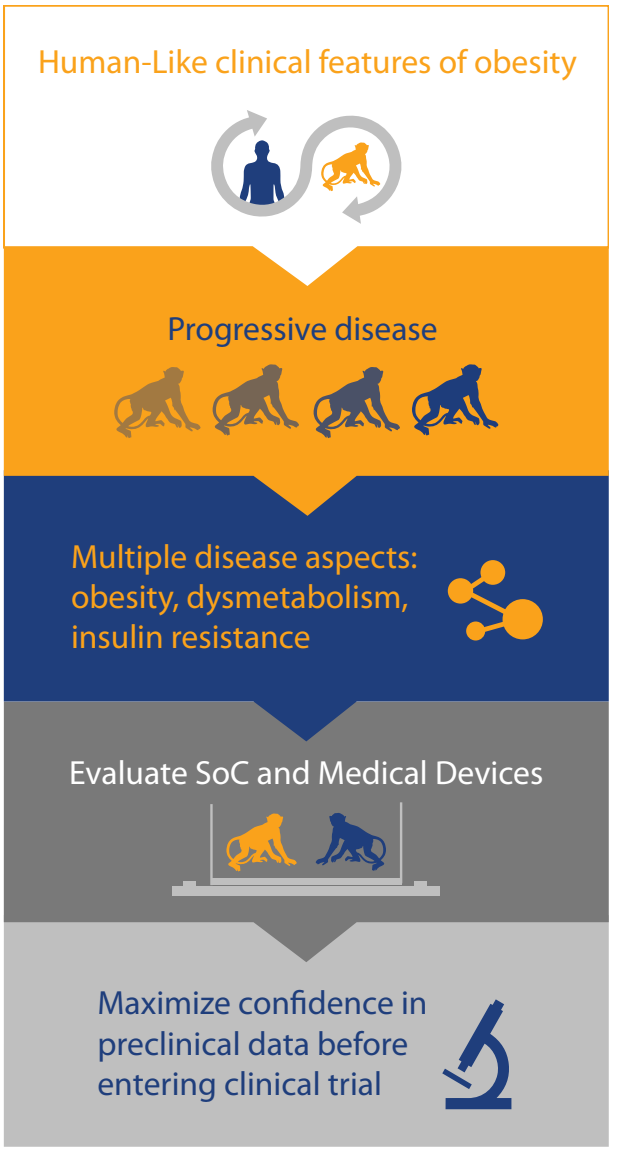
Discover how CrownBio's spontaneously dysmetabolic and obese NHPs provide highly predictive preclinical data to increase your chance of success in the clinic.

When making critical go/no-go decisions on anti-obesity agents entering clinical trials, it is important to use predictive data from human-relevant models. Non-human primates (NHPs) which naturally develop human metabolic syndrome are by far the most predictive preclinical models available for obesity studies.

- Exhibit human-like clinical features of obesity and dyslipidemia, as well as other dysmetabolic characteristics.
- Fully validated and well-characterized for all metabolic defects.
- Provide critical information to understand disease mechanisms, evaluate therapies, biomarkers, and medical devices, and to track human-like disease progression to complications.
- Maximize confidence in preclinical data before entering clinical trial.
- Diet-induced obesity models allowing research on diet effect in a range of dysmetabolic NHPs.



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Spontaneously Obese NHPs Key Facts

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CrownBio's well-characterized, naturally obese NHP models enable late-stage efficacy studies to inform clinical trials

- A cynomolgus and rhesus monkey colony, with the large colony size enabling consistent preclinical studies.
- Models mirror human disease clinical features of dysmetabolism e.g. obesity, insulin resistance, dyslipidemia, diabetes, and pancreatic pathology.
- Well-characterized models, through a range of assessments including weight, BMI, total fat measurements, and metabolic parameters (e.g. leptin levels, CRP, C-peptide).
- Highly translatable models to understand disease progression, and to evaluate novel agents and medical devices (e.g. noninvasive ultrasonography).
- Highly predictive late-stage data for go/no-go decisions to inform on which agents should move to clinical trial, providing a higher likelihood of success in the clinic.
- DIO models allowing research into the effects of diet in NHPs with various metabolic dysfunctions.

Spontaneously Obese NHPs – The Most Predictive Animal Model System for Human Metabolic Syndrome

CrownBio provides a large collection of cynomolgus and rhesus obesity NHP models, including both naturally occurring and experimentally induced disease models. Our naturally occurring NHP obesity model is the most translatable model for human disease, and can provide critical information for understanding disease mechanisms, evaluating therapies and biomarkers, and in tracking progression of obesity to other complications. When making important decisions about whether projects should proceed into the clinic, using the models that most closely mimic human dysmetabolism provides a distinct advantage, and maximum confidence in your results, reducing risk and increasing the chances of success in patients.

CrownBio's naturally occurring NHP obesity model exhibits in adulthood clinical features of obesity, insulin resistance, dyslipidemia, diabetes, and pancreatic pathology that are similar to those observed in humans, providing a highly translatable model. We have established criteria for grouping our in-house spontaneously obese NHPs fed a normal calorie diet, from lean to morbidly obese, based mainly on their total fat levels (**Table 1**).

Table 1: Grading of Spontaneously Obese NHPs

Total body fat measured with dual-energy x-ray absorptiometry (DXA) scan (GE Model: Lunar DPX-NT, Milwaukee, WI, USA).

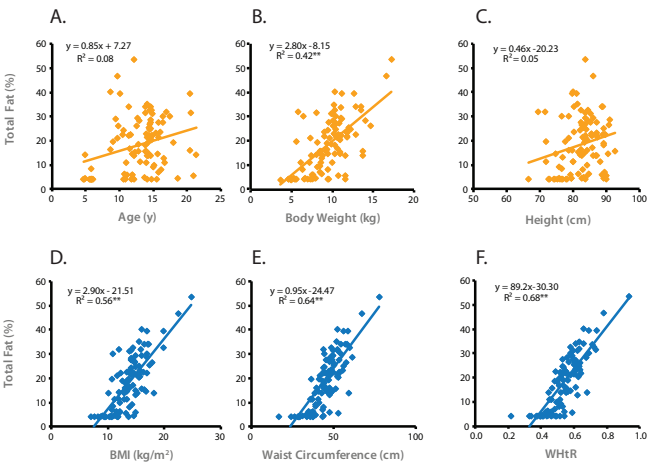
Grading	Total Fat (%)	Proportion of CrownBio Obese NHP Population (%)
Lean	≤10	29
Chubby	>10, ≤20	25
Obese	>20, ≤35	41
Morbidly Obese	>35	5

Well-Characterized and Fully Validated for Metabolic Defects

Animals in the obese groups are relatively older and show increases in their body weights, waist circumference, BMI, waist-to-height ratio (WHtR), and total percent fat compared with lean animals. Leptin levels in the obese and morbidly obese groups are significantly lower compared with the lean group, with most other metabolic parameters (e.g. CRP, C-peptide levels) remaining constant across the different animal groups. Total percent body fat levels of the spontaneously obese NHPs have been shown to significantly correlate with animal body weight, BMI, waist circumference and WHtRs, but not with age or height (**Figure 1**).

Figure 1: Correlations of Total Fat with Multiple Parameters in Spontaneously Obese Cynomolgus Monkeys

Correlation of total fat with A: age, B: body weight, C: height, D: BMI, E: waist circumference, F: WHtR.**p<0.01.



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Spontaneously Obese NHPs Factsheet

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Spontaneously Obese NHPs are Suitable Tools for Evaluating Therapies and Medical Devices for Human Metabolic Disease

As NHP models of obesity, dysmetabolism, and diabetes have been shown to be the most translatable animal model for human metabolic diseases, they are suitable tools for evaluating new therapies or medical devices in this field, including in fatty liver disease.

CrownBio has utilized our naturally obese NHPs to develop a noninvasive ultrasonography method for measurement of hepatic lipidosis and has demonstrated for the first time that, like human disease, these spontaneously obese NHPs develop liver disease with characteristics of NAFLD/NASH. We have also identified the interactions between the H/R ratio, HA, fibrosis indices, and metabolic disorders, which is consistent with human disease, confirming our obese NHP models as appropriate tools for medical device evaluation in this field.

Diet-Induced Obesity Models Allow Research into the Effects of Diet in NHPs with Various Metabolic Dysfunctions

Our models of spontaneous obesity are complemented by NHP models with high calorie diet (HCD) induced obesity. Our HCD comprises:

- Nutrient composition:
  - ≥16.3% protein
  - ≥17.7% fat
  - ≥1.9% fiber
  - 1.1% calcium
  - 0.6% phosphate
  - ≥0.5% cholesterol
- Energy source:
  - 16.2% protein
  - 39.5% fat
  - 44.3% carbohydrate.

Models have been generated from different groups of NHPs including lean and normoglycemic NHPs, obese, and diabetic monkeys to allow investigation and research within a variety of dysmetabolic disease types. For lean, normal NHPs with normoglycemia, relatively long term HCD causes significant increases in body weight, TC, TG, HDLc, and LDLc, but only affects blood glucose moderately (**Figure 2** and **Figure 3**). Body weight, food consumption, body composition, and blood biochemistry have also been studied in obese NHPs given an additional HCD. We have also validated the effects of HCD on metabolism in normoglycemic, pre-diabetic, and diabetic NHPs for the first time, providing initial information for those researching the effects of diet in animals with various metabolic dysfunctions.

Figure 2: Effects of a HCD on Food Intake and Body Weight of Lean and Normoglycemic NHPs

A: Changes in food intake (upper panel) and body weight (lower panel). B: Body weight changes in normal, lean NHPs fed with NCD, or with NCD and then HCD. HCD group n=94. NCD group n=18. *p<0.05, **p<0.01, ***p<0.001 vs pre-HCD baseline.

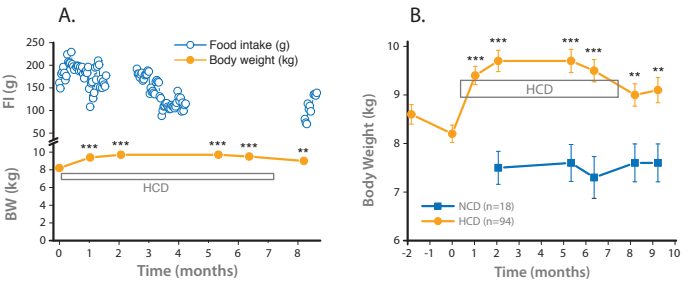

Figure 3: Effects of a HCD on Serum Glucose and Lipids of Lean and Normoglycemic NHPs

A: Changes in serum glucose in normal NHPs fed with NCD only or with HCD. B: Comparison of serum TC, TG, HDLc, and LDLc in NCD-only NHPs with those fed with HCD for over 7 months. HCD group n=94. NCD group n=18. *p<0.05, **p<0.01, ***p<0.001 vs pre-HCD baseline or vs control in Panel B.