Insulin Resistance in Old World Primates

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Introduction

A recent survey of diabetes in zoo primates found that approximately one third of zoos report housing diabetic primates (Kuhar et al., in prep). Old world monkeys comprised ~50% of total diabetes cases and prosimians comprised ~13% of all cases (Kuhar et al., in prep). It is currently unknown what risk factors precede development of this disease in nonhuman primates. In humans, type II diabetes is often preceded by a state of insulin resistance (Martin et al., 1992). Insulin resistance is a condition in which the body produces insulin but tissues, specifically muscle, fat and liver cells, do not appropriately respond to the presence of insulin with the uptake and utilization of glucose. In humans, insulin resistance syndrome (also known as metabolic syndrome) is defined in a patient as having three of the following criteria: increased waist circumference, increased serum triglycerides, reduced HDL, increased blood pressure, and increased fasting blood glucose (Grundy et al., 2004). The World Health Organization adds increased serum insulin levels as a criterion to this syndrome (Beilby, 2004). Although studies have examined one-time point samples of several of these biomarkers in nonhuman primates, there have been no studies examining how these serum biomarkers might change in one individual over time.

Hypothesis: Serum biomarkers of insulin resistance increase over time preceding the development of type II diabetes.

Specific aims: To determine the effect of increasing age/time spent in captivity on insulin, glucose, cholesterol and triglycerides in banked serum samples from one species of ape: orangutans, two species of old world monkey: Hamadryas baboons and mandrills and two species of prosimian: ring-tailed and red ruffed lemurs.

Subjects: Individuals with known diagnosis of type II diabetes, known absence of type II diabetes and unknown diagnosis of type II diabetes will be included from the following species: orangutans, Hamadryas baboons, mandrills, ring-tailed lemurs and red ruffed lemurs.

Methodology: A minimum of 3 and maximum of 6 banked serum samples for each individual will be analyzed for insulin, glucose, cholesterol and triglycerides. A commercially available enzyme-linked immunosorbent assay (ELISA) kit will be used to analyze serum insulin (Mercodia, 10-1132-01). This assay was previously validated for use with serum for the above listed species in the Cleveland Metroparks Zoo Endocrinology Laboratory. Serum glucose, cholesterol and triglycerides will be measured using an IDEXX vettest autoanalyzer. If available, up to 6 samples per individual are requested, but a minimum of 3 samples are required. The type of anesthetic used will be noted for all serum samples.

A meta-analysis of correlation coefficients for each individual will be used to compare fasting serum concentrations of all biomarkers over time. We will control for species type, sex, age, family history (if known) and change in weight in all analyses. Significance for all statistical tests will be set at $p < 0.05$.

Timeline: All samples will be run in the CMZ's endocrinology laboratory by December 2012.

Budget: All funds provided by CMZ.

Expected outcomes: We expect to see a concurrent increase in serum insulin, cholesterol, and triglycerides if serum glucose is increasing.

Significance: If insulin resistance syndrome does appear to increase over time or precede the development of type II diabetes, zoological managers and veterinarians can assess individual primates for insulin resistance and intervene prior to the development of overt disease. Type II diabetes is difficult to diagnose as the stress of the anesthesia process can raise serum glucose levels potentially providing misleading information. Although other serum biomarkers can be altered depending on the anesthetic used and by the exam process, examining multiple serum biomarkers in multiple serum samples from one individual will help create a clearer picture of what is happening metabolically. This study could have important implications for managing the health of old world primates in zoos.

Checklist of information needed for this study:

- 3-6 serum samples per individual, each at least 2 ml
- Medical records pertaining to the time period of the samples
- Weights corresponding to the serum samples (if not available in the records)
- Diets corresponding to time period of the serum samples