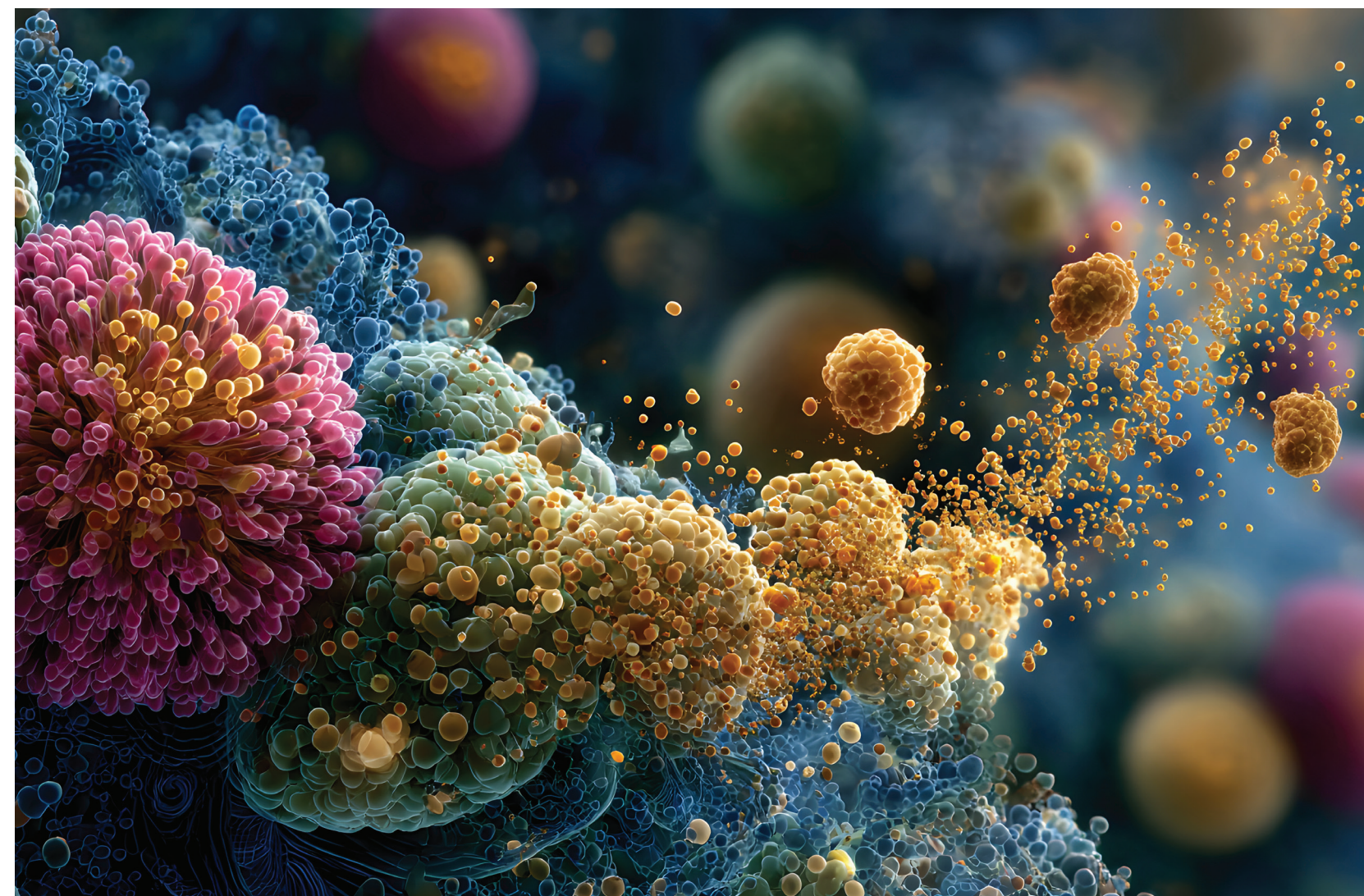




**Characterization of a Colony of Cynomolgus Monkeys
to Support Metabolic Disease Drug Development**

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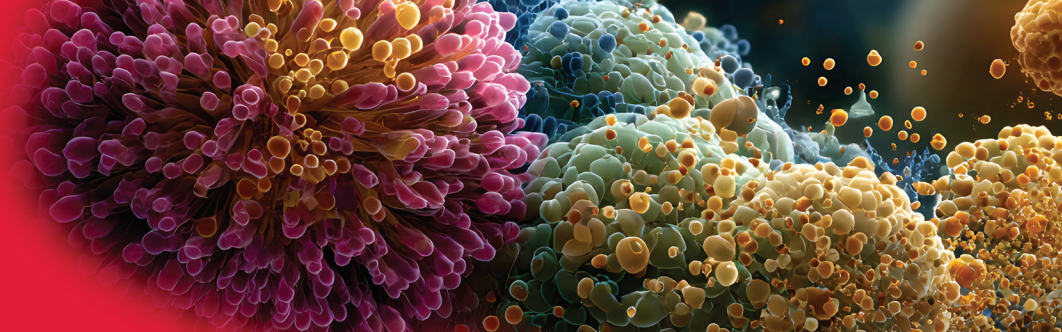
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Characterization of a Colony of Cynomolgus Monkeys to Support Metabolic Disease Drug Development

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INTRODUCTION

Biomere has the largest nonhuman primate (NHP) facility in New England that includes a diverse population from different origins. The onsite colony undergoes routine exams that includes body weight, body condition score and clinical chemistry analysis. The biochemical profiles of NHPs can be impacted by several factors including but not limited to sex, age, body weight and origin.

In this study, we evaluated the variability of Complete Blood Counts (CBC) and chemistry panels in a population of 316 NHPs. When determining which factors to consider targeting as the independent variables for chemistry data we first looked at the over arching variety within the colony as shown in Figure 1. Each age group was then assessed for average body weight to normalize data further referred to as “body weight index” (BWI) and analytes were analyzed for apparent trends.

NHP COLONY CHARACTERISTICS DISTRIBUTION

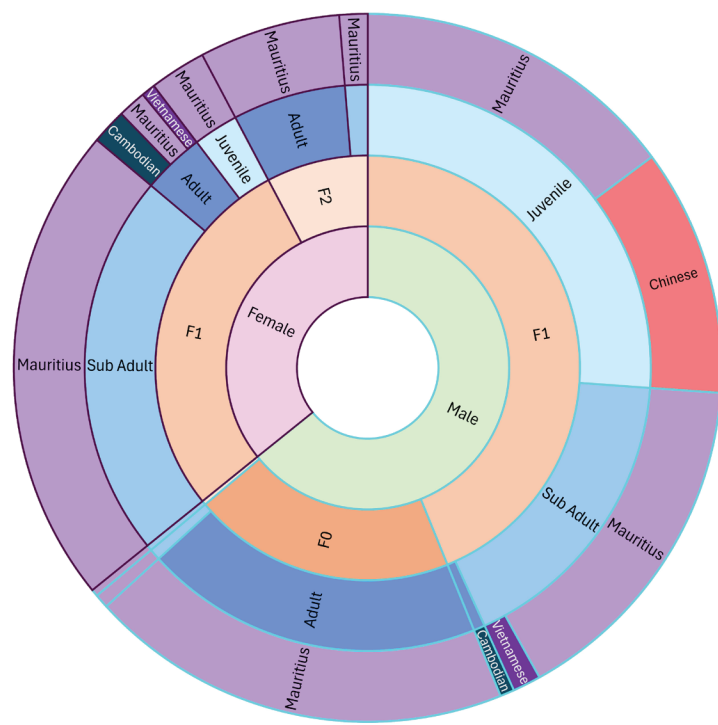


Figure 1: Hierarchical composition of NHP population, showing individuals distributed across gender, generation, age group and origin.

~63% Male, ~37% Female
~70% F1 Generation, ~20% F2 Generation
~28% Juvenile, ~42% Sub-Adult, ~29% Adult
~85% Mauritius Origin, ~15% Asian Origin

GLUCOSE REGULATION

Triglyceride glucose (TyG) index was calculated and assessed for insight into potential insulin resistance among the colony (Figure 2). However, there was no statistically significant difference in TyG in the cohorts with different body weight indices (BWI). It is important to note that, as expected, there were increased triglycerides in adult animals compared to juveniles but however, variables such as fasting time and sedation agent, were not accounted for in this assessment.

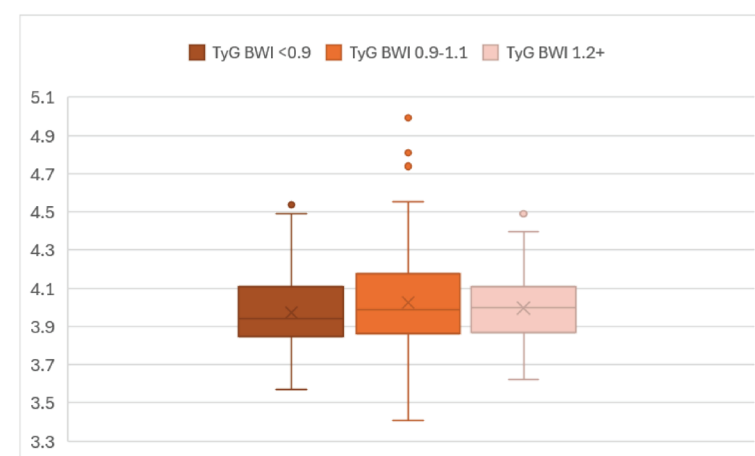


Figure 2. Triglyceride glucose (TyG) index as compared to BWI in NHP population

CBC MARKERS

When focusing in on origin we can visualize the alternative erythrocyte levels between our Chinese and Mauritius origin NHPs. Chinese origin NHPs have on average a lower RBC count; with a higher hemoglobin (HGB) density as compared to Mauritius NHPs (Figure 5). This suggests that the Mauritius animals have smaller RBCs with less hemoglobin per cell whereas Chinese origin have fewer, larger RBCs with more hemoglobin per cell. This is supported when assessing hematocrit % (HCT) which on average is not significantly different in comparison.

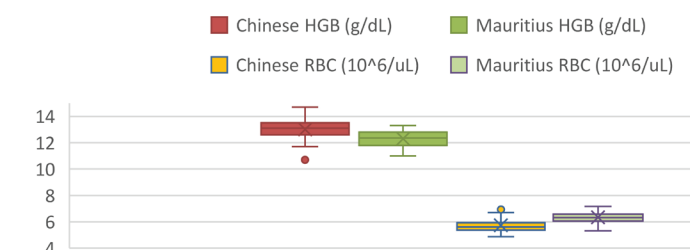


Figure 5. Comparison of RBC and HGB in juvenile cynomolgus macaques based on origin.

LIVER METABOLISM

Stress on the liver from fat accumulation can be extrapolated from ALT, AST and GGT (gamma-glutamyl transferase) levels. ALT levels in combination with AST levels are used to assess chronic vs acute hepatic stress. As shown in Figure 3, in juvenile NHPs there is a positive correlation between body weight scoring and the ALT:AST Ratio. Interestingly, all the outliers were of Chinese origin suggesting that Chinese origin NHPs may be susceptible to higher hepatic stress.

GGT levels is indicative of lipid metabolism and oxidative stress so increased levels of GGT suggests that the liver or bile ducts are under stress. There is a positive correlation between BWI and GGT; suggesting animals with higher body weight scoring for their age pool may have a pre-disposition to develop fatty liver (Figure 4).

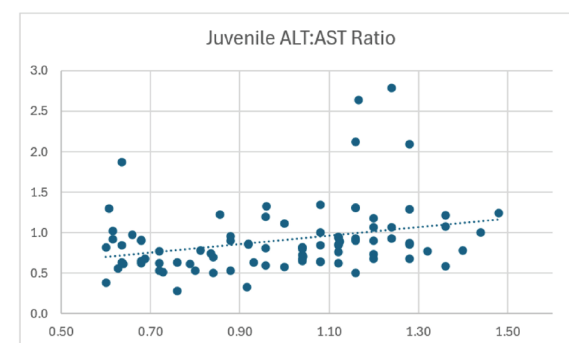


Figure 3. Weak positive correlation between BWI and ALT:AST ratio in Juvenile NHPs

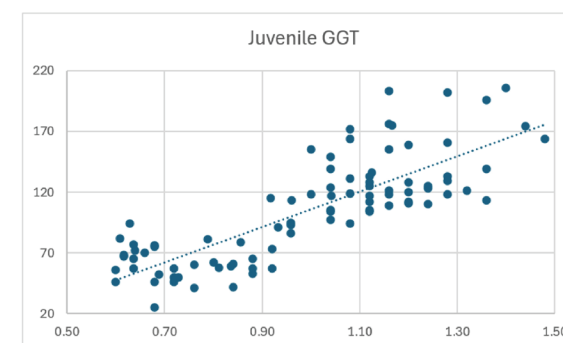


Figure 4. Strong positive correlation between BWI and GGT levels in Juvenile NHPs

SUMMARY

In summary, routine examination of Biomere's onsite NHP colony that includes body weight scoring, biochemical markers and CBCs provides valuable data to refine animal selection for studies focused on specific disease areas such as fatty liver, obesity and metabolic dysfunction. Additionally, this data promotes proactive colony management for preventative care to ensure high levels of animal welfare.

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