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The Critical Role of Mauritian Cynomolgus Macaques in Drug Discovery and Development

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1. Introduction

Mauritian cynomolgus macaques ("Macaca fascicularis" or "MCM") have emerged as a critical resource in biomedical research. Their unique genetic profile, low pathogen burden, and well-characterized immune systems make them indispensable for drug discovery, preclinical safety, and translational research.

2. Historical Context and Population Genetics

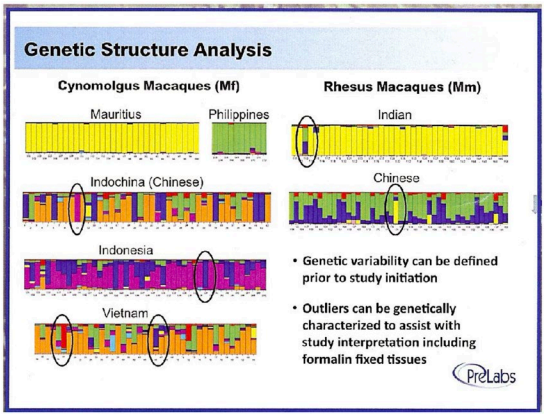
- Introduced to Mauritius 400 years ago from Southeast Asia.
- Not endemic to Mauritius – a significant difference from Asian NHPs
- Use of Mauritian NHPs aids biodiversity enhancement in Mauritius.
- Genetic studies (Bonhomme et al., 2008; Osada et al., 2015) confirmed an estimated founder population of 10-20 animals.
- Low mitochondrial and nuclear diversity (Badhan et al., 2015; Blancher et al., 2008), enhancing reproducibility in research.

MCM is a pure Cynomolgus with no hybridization

- MCM is a pure Cynomolgus from only one subspecies with no hybridization with other subspecies or other macaque species – unlike Asian NHPs
- There are 10 different known subspecies of Macaca Fascicularis in Asia – resulting in a difference in many physiological and genetic aspects
- Hybridization in Asia occurs in between subspecies of Macaca Fascicularis and also within subspecies and with other macaque species (Rhesus, Pig tail ..)
- This hybridization is creating a different animal model with a variety of reproductive, physiological and genetic structures

3. Immunological and Genetic Advantages of Mauritian NHPs

- Simplified MHC haplotype diversity (Burwitz et al., 2009), facilitating immunological studies and vaccine development.
- Characterized Fcγ receptor diversity (Haj et al., 2019) improves antibody/biologic therapy evaluations.
- Unique genomic resources including fully assembled KIR and NKG2 haplotypes (Prall et al., 2024) enhance immunological profiling.



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4. Health and Pathogen-Free Status

- Historically low exposure to endemic pathogens (Matsubayashi et al., 1992).
- Unique discovery of chronic HBV infection (Dupinay et al., 2013) provides a natural model for chronic hepatitis research.

Naturally Born SPF Animals

- All Mauritian-origin primates are naturally born SPF (B-virus, SRV, SIV, STLV1 free) with no seroconversion.
- 100% of animals and offspring are SPF.
- Asian-origin animals in research have tested negative but later became positive under stress or immune compromise, which does not occur in Mauritian Cynomolgus.
- Ideal for drug discovery helping alleviate safety concerns for researchers and animal caregivers.

5. Physiological and Developmental Superiority of Mauritian NHPs

- Faster sexual maturity (Luetjens et al., 2012).
- Consistent hematological and biochemical reference intervals (Bonfanti et al., 2009; Naiken et al., 2016).
- Lower incidence of spontaneous pathology compared to Asian-origin macaques (Kozlosky et al., 2015; Chamanza et al., 2022).

Genetically Homogeneous Animals

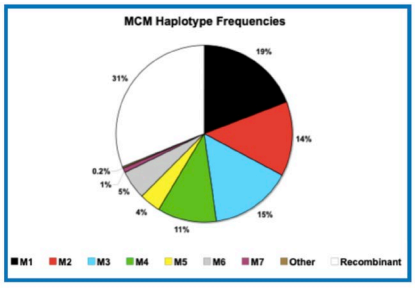
- Mauritian-origin primates are genetically homogeneous, unlike their Asian counterparts.
- Studies demonstrate clear advantages in consistency and reliability for biomedical research.
- Outliers can be genetically characterized to assist with data interpretation.

6. Translational Relevance in Preclinical Research

- Highly predictive PK/PD profiles (Kozlosky et al., 2015).
- Genetic homogeneity reduces variability in drug response.
- Validated for use across drug modalities, from small molecules to biologics and gene therapies.

MHC Haplotype Advantage

- Mauritian cynomolgus macaques exhibit ~8 distinct haplotypes (M1-M7 + recombinant).
- Selective breeding enables MHC-defined groups for transplantation, vaccine studies, and biomedical research.
- Rhesus macaques, by contrast, have dozens of haplotypes with multiple variants, making research more complex.



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7. Comparisons with Asian-Origin Cynomolgus Macaques

Parameter	Mauritian Origin	Asian Origin (Cambodia, China, Vietnam)
Genetic Diversity	Low (homogeneous)	High (heterogeneous)
Pathogen Burden	Low (SPF status)	Higher exposure to endemic pathogens
Reproductive Maturity	Faster onset	Delayed compared to Mauritian origin
Spontaneous Pathology	Lower incidence	Higher incidence in digestive and lymphoid systems
Translational Consistency	High	Variable

8. Mauritian F1 Vs F0 NHP

A key driver on the price of any NHP study is whether the animal used on-study is island-bred (F0 or wild caught) or bred in captivity (F1 or F2). The capture of animals from the wild and exported for research is illegal in Asia. This is not the case in Mauritius, since the NHPs are not endemic to the island. Doing so helps foster the island's biodiversity which was devastated prior to providing this valuable resource for research to the world.

Importantly, Mauritian, F0 NHPs made possible by our partner, Bioculture Mauritius, is that animals are first acclimated and socialized in captivity for at least 12-14 months prior to being exported to the US. Many of the F0s also come in as babies with their mothers and hence spend all their lives as captive bred NHPs prior to being placed on studies.

Studies have shown no difference in clinical pathology parameters between F0 and F1 animals. It is also highly unlikely that there would be a difference in PK/PD of a drug in a F0 vs F1 NHP, however, there is nothing in the literature to support this, yet. Studies are currently being designed to test this hypothesis. Should the data support our contention, we will be in a unique position to provide clients with the most cost-effective and time-efficient service in the industry for drug discovery.

9. Supply Chain and Ethical Sourcing

- COVID-19 highlighted fragility of Asian supply chains.
- Mauritius offers a stable, legally regulated supply with clear chain of custody.

10. Conclusion

Mauritian cynomolgus macaques combine genetic simplicity, physiological consistency, pathogen-free status, and reliable supply, making them the gold standard NHP model for drug development and safety assessment.

Mauritian cynomolgus macaques also provide an option between F2, F1, and F0 NHPs which is unique and can significantly bring down the time and cost of studies.

11. References

- **Matsubayashi et al., 1992:** Conducted clinical examinations of wild-caught Mauritian macaques, confirming excellent baseline health and minimal natural infections. This paper was foundational in highlighting their SPF-like status.
- **Lawler et al., 1995:** Demonstrated the mitochondrial DNA bottleneck effect in Mauritian macaques. This study confirmed their Indonesian origin and the strong genetic uniformity caused by the founding event.
- **Bonhomme et al., 2008:** Used nuclear microsatellite data to reconstruct population history and estimated a founder population of just 10-15 individuals. This paper emphasized the importance of this genetic simplicity for biomedical reproducibility.
- **Blancher et al., 2008:** Conducted phylogenetic analyses of mitochondrial DNA from multiple populations, reaffirming the low genetic diversity in Mauritian macaques.
- **Burwitz et al., 2009:** Identified the two most common MHC class I alleles in Mauritian macaques and showed that they restrict key CD8+ T-cell responses. This work highlights the uniformity in immune responses.
- **Bonfanti et al., 2009:** Compared hematological and serum chemistry values between wild-caught and purpose-bred Mauritian macaques. This paper established key clinical reference intervals.
- **Naiken et al., 2015, 2016:** Conducted extensive biochemical and hematological profiling in juvenile Mauritian macaques. This data is used widely in preclinical research.
- **Osada et al., 2015:** Performed whole genome sequencing on Mauritian macaques, documenting reduced polymorphism and confirming Indonesian ancestry.
- **Kozlosky et al., 2015:** Compared physiology, drug metabolism, and immunological parameters across different macaque populations, highlighting the stability and consistency of Mauritian-origin animals.
- **Dupinay et al., 2013:** Discovered naturally occurring chronic hepatitis B virus in Mauritian macaques, which can serve as a unique preclinical model for human HBV.
- **Haj et al., 2019:** Characterized Fc receptor alleles in Mauritian macaques, demonstrating limited diversity, which simplifies antibody-based research.
- **Chamanza et al., 2022:** Comprehensive review of spontaneous histopathology in laboratory cynomolgus macaques, documenting that Mauritian animals show fewer inflammatory and degenerative changes.
- **Prall et al., 2024:** Completed the first full genomic assembly of KIR and NKG2 haplotypes in Mauritian macaques, providing invaluable immune-genetic data.