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Development of Non-Human Primates as Translational Models

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ABSTRACT: To test the efficacy, pharmacokinetics and safety of a drug for a particular human disease, a good animal model is desired before the drug goes into clinical trials. These prototypes thus need to be mimicking the human disease phenotype as well as the underlying causations. This is a tough scenario as in most of the cases the rate of effective translation from animal models to clinical trials is less very low. This is so due to the non-clarity and the gap in understanding the differences between these models and humans. In order to develop experimental models of human disease and test novel therapeutic interventions, non-human primate (NHP) models provide distinct advantages, particularly for metabolic disorders.To fully leverage on using NHP for translational research, the suitability of NHP using biomarkers should be thoroughly explored to narrow the gap in understanding the differences. Cynomolgus monkeys were considered as models for dyslipidemia/atherosclerosis. Several diets were tested and were characterized. Various LC-MS and cell based assay were developed and applied to fully characterize these monkeys on high fat diets. These assays included lipid profiling using clinical chemistry, cholesterol synthesis using tracer studies, cholesterol absorption, HDL functionality and other novel biomarkers. These markers have been shown to be clinically relevant thus demonstrating the translatability of NHP models.

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