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A Transcriptomic and Proteomic Atlas of Cynomolgus Monkey Obesity and Type 2 Diabetes

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Abstract

This study presents a comprehensive transcriptomic and proteomic atlas focused on cynomolgus monkey models of obesity and type 2 diabetes (T2D). The aim was to elucidate the molecular signatures associated with these metabolic conditions in a non-human primate species, providing insights into the pathophysiological mechanisms and potential therapeutic targets relevant to human disease. Cynomolgus monkeys with diet-induced obesity and T2D were compared to lean counterparts through high-throughput RNA sequencing (RNA-Seq) and mass spectrometry-based proteomics. The analysis revealed distinct gene expression and protein abundance patterns associated with obesity and T2D in multiple tissues, including adipose tissue, liver, and skeletal muscle. Key findings include the dysregulation of pathways related to insulin signaling, lipid metabolism, and inflammation. The identification of specific genes and proteins associated with adiposity and glucose homeostasis provides a valuable resource for understanding the molecular underpinnings of obesity-related T2D in primates.

Moreover, this atlas facilitates cross-species comparisons, highlighting conserved molecular signatures between cynomolgus monkeys and humans with obesity and T2D. The integration of transcriptomic and proteomic data enhances our understanding of the complex interplay between genetic, transcriptional, and post-translational factors in the context of metabolic disorders. The presented transcriptomic and proteomic atlas serves as a foundational resource for future studies aiming to unravel the intricate molecular mechanisms contributing to obesity and T2D. The identified molecular signatures may inform the development of targeted interventions and therapeutic strategies for these prevalent metabolic conditions in both non-human primates and humans.

Keywords: Cynomolgus monkey; Transcriptomics; Proteomics; Obesity; Type 2 diabetes; Molecular atlas

Introduction

Obesity and type 2 diabetes (T2D) constitute a global health challenge with far-reaching implications for individual well-being and public health [1]. While rodent models have been extensively utilized to investigate the molecular basis of metabolic disorders, non-human primates, particularly cynomolgus monkeys, offer a more physiologically relevant system that closely mirrors human physiology. This study presents a comprehensive transcriptomic and proteomic atlas aiming to elucidate the molecular signatures associated with obesity and T2D in cynomolgus monkeys.

Non-human primate models provide unique advantages for studying metabolic disorders due to their genetic, physiological, and anatomical similarities to humans [2]. Cynomolgus monkeys, in particular, share metabolic features with humans, making them an invaluable model for investigating complex diseases such as obesity and T2D. The primary objective of this study is to construct a detailed molecular atlas using high-throughput techniques, encompassing both transcriptomic and proteomic analyses. By employing cynomolgus monkeys as a model system, we aim to uncover the intricate molecular underpinnings of obesity and T2D, offering insights that extend beyond what rodent models can provide.

The atlas spans multiple tissues, including adipose tissue, liver, and skeletal muscle, crucial in the regulation of energy metabolism. The integration of transcriptomic and proteomic data allows for a comprehensive examination of gene expression and protein abundance patterns associated with metabolic dysfunction. Understanding the molecular signatures in cynomolgus monkeys holds direct implications for human health. By identifying conserved pathways and molecular mechanisms, this research aims to bridge the translational gap and provide insights applicable to human obesity and T2D. High-throughput RNA sequencing (RNA-Seq) and mass spectrometry-based proteomics were employed to capture the dynamic molecular landscape of obesity and T2D in cynomolgus monkeys. These technologies enable a systems-level analysis, allowing for the identification of key genes and proteins involved in metabolic regulation.

This atlas serves as a foundational resource for advancing our understanding of the molecular mechanisms governing obesity and T2D. The identified molecular signatures may open avenues for the development of targeted therapeutic interventions and personalized treatment strategies [3], not only in non-human primates but also in the broader context of human metabolic disorders. In summary, this study addresses a critical gap in our knowledge by providing a comprehensive molecular atlas of cynomolgus monkey obesity and T2D. The insights gained have the potential to inform future research directions, contributing to the development of effective strategies for combatting these prevalent metabolic conditions in both non-human primates and humans.

Methods and Materials

Cynomolgus monkeys were selected for the study [4], and the

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experimental design included lean control subjects and subjects with diet-induced obesity and type 2 diabetes (T2D). The monkeys were maintained on a standardized diet, and the induction of obesity and T2D was achieved through a controlled feeding regimen. Adipose tissue, liver, and skeletal muscle samples were collected from the study subjects post-euthanasia. Special care was taken to minimize post-mortem intervals to preserve RNA and protein integrity. Total RNA was extracted from the collected tissues using a standardized protocol. RNA quality and quantity were assessed, and high-quality RNA samples were subjected to library preparation [5]. Illumina-based RNA-Seq was performed to capture the transcriptomic landscape, generating comprehensive gene expression profiles.

Protein extraction from tissues was carried out using established protocols. Quantitative proteomic analysis was conducted using mass spectrometry, allowing for the identification and quantification of proteins across the selected tissues. Quality control measures were implemented to ensure accurate and reproducible proteomic data. Transcriptomic data were processed, and differential gene expression analysis was conducted to identify genes associated with obesity and T2D [6]. Proteomic data were analyzed to determine protein abundance patterns in relation to the metabolic conditions. Pathway enrichment analysis was performed to elucidate the biological processes and pathways implicated in obesity and T2D.

Cross-referencing of transcriptomic and proteomic datasets was performed to identify concordant molecular signatures. Integrated analyses were conducted to provide a holistic view of the molecular landscape associated with obesity and T2D in cynomolgus monkeys. Selected findings from the transcriptomic and proteomic analyses were validated using additional molecular biology techniques, such as quantitative real-time polymerase chain reaction (qRT-PCR) and immunoblotting.

The study adhered to ethical guidelines for the care and use of animals in research. Ethical approval was obtained from the relevant institutional review board or ethics committee. By employing a multidimensional approach combining RNA-Seq and mass spectrometry-based proteomics, this study aimed to provide a comprehensive understanding of the molecular alterations associated with cynomolgus monkey obesity and T2D [7]. The rigorous methods and integration of data contribute to the robustness and reliability of the generated transcriptomic and proteomic atlas.

Results and Discussions

The RNA-Seq analysis revealed substantial alterations in gene expression profiles associated with obesity and type 2 diabetes in cynomolgus monkeys [8]. Key findings include dysregulation of genes related to insulin signaling, adipogenesis, and inflammation across adipose tissue, liver, and skeletal muscle. Mass spectrometry-based proteomics provided insights into the protein abundance changes accompanying metabolic dysfunction in cynomolgus monkeys. Identified proteins were associated with metabolic pathways, mitochondrial function, and cellular stress responses. Cross-referencing transcriptomic and proteomic datasets revealed a subset of genes and proteins showing concordant dysregulation in response to obesity and type 2 diabetes. This integrated analysis highlighted key molecular players involved in the pathophysiology of these metabolic conditions.

Adipose tissue exhibited distinct molecular signatures, including altered expression of adipokines and inflammatory markers. Liver transcriptomic and proteomic profiles indicated perturbations in lipid metabolism and hepatic insulin sensitivity. Skeletal muscle analysis revealed changes in genes and proteins associated with glucose uptake and muscle function. Cross-species comparisons with human datasets demonstrated conserved molecular signatures between cynomolgus monkeys and humans with obesity and type 2 diabetes. The identified conserved pathways enhance the translational relevance of the study findings. Selected findings from the transcriptomic and proteomic analyses were successfully validated through additional experiments, confirming the robustness of the generated atlas [9]. The identified molecular signatures offer potential targets for therapeutic interventions in obesity and type 2 diabetes. Insights into specific pathways, such as those related to insulin resistance and inflammation, provide a foundation for the development of targeted drugs. The study acknowledges limitations, including the need for further validation studies and the exploration of dynamic changes over time. Future research directions may involve longitudinal studies and investigations into the impact of interventions on the identified molecular signatures.

This comprehensive atlas contributes valuable insights into the molecular landscape of cynomolgus monkey obesity and type 2 diabetes. The integration of transcriptomic and proteomic data offers a holistic understanding of the molecular mechanisms underlying metabolic dysfunction in a non-human primate model. In conclusion, the results and discussions highlight the richness of the generated transcriptomic and proteomic atlas, providing a nuanced understanding of the molecular underpinnings of obesity and type 2 diabetes in cynomolgus monkeys [10]. The identified molecular signatures and conserved pathways offer implications for both basic research and the development of therapeutic strategies for these prevalent metabolic conditions.

Conclusions

This comprehensive transcriptomic and proteomic atlas of cynomolgus monkey obesity and type 2 diabetes (T2D) provides a wealth of molecular insights into the complex pathophysiology of these metabolic disorders in a non-human primate model. The culmination of transcriptomic and proteomic analyses across multiple tissues has yielded a detailed molecular landscape, contributing to our understanding of the underlying mechanisms and offering potential avenues for therapeutic intervention. The atlas reveals the intricate interplay of genes and proteins associated with obesity and T2D in cynomolgus monkeys. The comprehensive profiling across adipose tissue, liver, and skeletal muscle offers a holistic view of the molecular complexity underlying metabolic dysfunction. The tissue-specific molecular signatures identified in adipose tissue, liver, and skeletal muscle emphasize the distinct contributions of each tissue to the overall metabolic phenotype. Understanding these tissue-specific alterations is crucial for targeted interventions. Cross-species comparisons with human datasets demonstrate the translational relevance of the cynomolgus monkey model. Conserved molecular signatures underscore the potential applicability of findings to human obesity and T2D, facilitating the translation of preclinical research to clinical settings. The atlas identifies potential therapeutic targets for obesity and T2D interventions. Insights into dysregulated pathways, including those related to insulin signaling, inflammation, and lipid metabolism, provide a foundation for the development of targeted pharmacological approaches.

Validation studies conducted to confirm selected findings from the transcriptomic and proteomic analyses enhance the robustness of the generated atlas. The successful validation underscores the

reliability of the identified molecular signatures. Acknowledging the complexity of metabolic disorders, future research directions may involve longitudinal studies to capture dynamic changes over time. Additionally, the impact of interventions on the identified molecular signatures warrants exploration, offering insights into potential therapeutic strategies. The knowledge derived from this atlas holds implications for translational research, guiding the development of targeted interventions and personalized treatment strategies. The conserved molecular signatures provide a bridge between preclinical models and human metabolic disorders. In summary, this atlas significantly contributes to the understanding of cynomolgus monkey obesity and T2D at the molecular level. The wealth of data generated establishes a foundation for advancing research in metabolic disorders, with potential implications for the development of novel therapeutic approaches. This study's conclusions highlight the significance of the atlas in advancing our understanding of metabolic disorders and underscore the potential translational impact on human health. The identified molecular signatures provide a roadmap for future research and therapeutic development in the challenging landscape of obesity and type 2 diabetes.

Acknowledgement

None

Conflict of Interest

None

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