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Definitions

- **Splicing Factor (SF)**: Proteins that help in the process of cutting and joining RNA to form mature mRNA.
- **Alternative Splicing (AS)**: A process where different parts of an RNA transcript are joined in different ways to produce multiple protein variants.
- **Non-Alcoholic Fatty Liver Disease (NAFLD)**: A condition where fat builds up in the liver without alcohol use.
- **Polychlorinated Biphenyls (PCBs)**: Toxic chemicals found in the environment that can cause health problems.
- **High-Fat Diet (HFD)**: A diet that consists of a high percentage of calories from fats.

Key Findings

- PCB exposure changes the expression of splicing factors and alternative splicing events in the liver.
- These changes can lead to altered gene expression and may contribute to liver disease.
- Co-exposure to different types of PCBs with a high-fat diet resulted in significant changes in splicing factors and alternative splicing events.

Introduction

The study investigates how exposure to PCBs and a high-fat diet affect the liver at the molecular level, specifically looking at splicing factors and alternative splicing events. Understanding these changes can help explain how environmental toxins contribute to liver diseases like NAFLD and NASH.

Main Content

Background

NAFLD is a common liver disease linked to obesity and poor diet. PCBs are harmful chemicals that can worsen liver conditions. This study examines how these factors alter RNA splicing in the liver, which can lead to changes in gene expression and disease progression.

Methods

- **Animal Studies**:

- Adult male mice were fed a high-fat diet and exposed to different types of PCBs.
- The mice were divided into groups: control (no PCB), Aroclor1260, PCB126, and a combination of Aroclor1260 and PCB126.
- Liver tissues were collected for analysis after 12 weeks.

- **RNA Analysis**:
  - mRNA sequencing was used to study RNA splicing changes.
  - The replicate multivariate analysis of transcript splicing (rMATS) identified different splicing events.
  - Western blotting confirmed the changes in splicing factor protein levels.

Results

- **Splicing Factor Changes**:
  - Co-exposure to Aroclor1260 and PCB126 altered the expression of 101 splicing factors.
  - Specific proteins, like DDX3X and SART1, showed significant changes in abundance.
- **Alternative Splicing Events**:
  - 449 alternative splicing events in 366 genes were identified with co-exposure to Aroclor1260 and PCB126.
  - These events included different types like skipped exons and mutually exclusive exons.
- **Functional Impact**:
  - Changes in splicing were linked to important liver functions, including lipid metabolism and inflammation.
  - m6A RNA modifications were associated with these splicing changes, suggesting a regulatory mechanism.

Conclusion

The study demonstrates that PCB exposure and a high-fat diet significantly impact RNA splicing in the liver, leading to changes in gene expression that may contribute to the progression of liver diseases like NAFLD. Understanding these mechanisms can help in developing strategies to prevent or treat liver disease caused by environmental toxins.

Word Count: 460