

The Effect of the Regulation of Gene CD163 In NASH vs Normal Weight Patients

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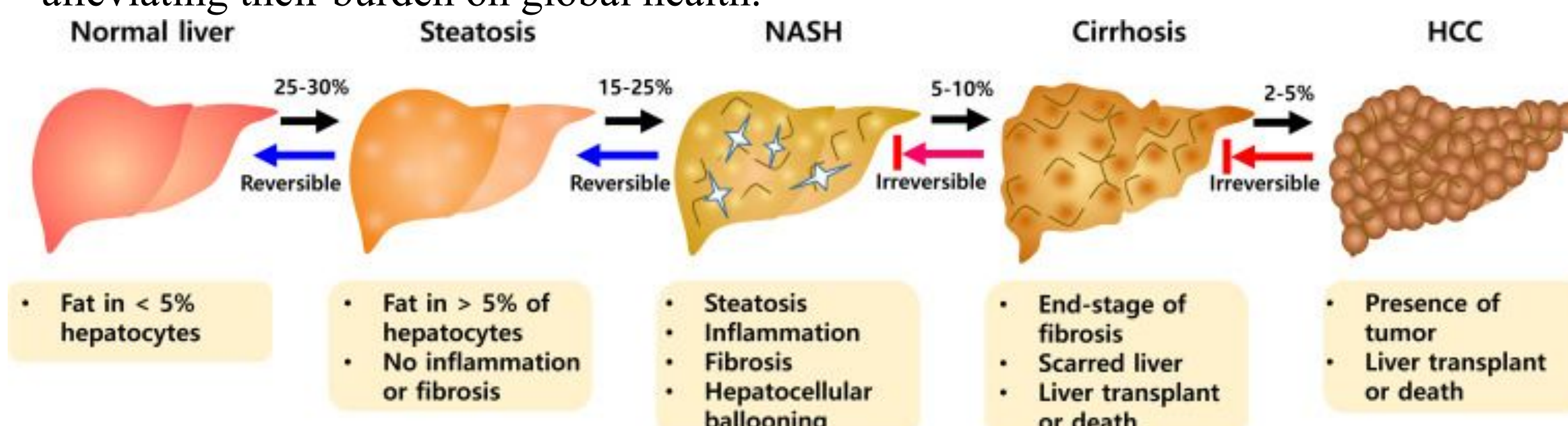
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Abstract: Non-alcoholic fatty liver disease (NAFLD) has become more common worldwide due to increasing obesity rates. NAFLD symptoms include inflammation, insulin resistance, and changes in gut bacteria. Unfortunately, there aren't many effective treatments available for NAFLD. However, recent studies have shown that bile acids (BAs) play a significant role in NAFLD and its more severe form, non-alcoholic steatohepatitis (NASH). Therefore this study will dive deeper into reviewing those studies and gather data to conclude to a step further in finding a effective therapy to this growing disease. In order to gather data, This research focused on analyzing the GEO2R of data published on pubmed, which focused on different genes that correlated between NASH and Normal weight. The study found one gene CD163 was significantly expressed differently than amongst many others. This gene was triple in Normal weight than NASH. many research studies have found that CD163 is elevated when found in obese patients therefore It was hypothesized that CD163 would be upregulated in NASH as well. In summary, many studies are still in the process of finding effective therapies for NASH that have to do with peculiar genes as CD163, therefore this study was just a small step in that processes.

Introduction

Non-alcoholic fatty liver disease (NAFLD) and its progressive form, non-alcoholic steatohepatitis (NASH), have emerged from significant global health concerns in recent years. NAFLD encompasses a range of liver disorders characterized by the accumulation of excessive fat in hepatocytes, an important tissue type in the liver, unrelated to significant alcohol consumption. NASH represents a more severe subtype, marked by inflammation, hepatocellular injury, and fibrosis. In the quest to understand the molecular intricacies underlying NAFLD and NASH, attention has increasingly turned towards bile acids. Mainly bile acids are known for their involvement in lipid digestion and absorption. However bile acids have emerged as crucial regulators of liver homeostasis and key players in the pathogenesis of these diseases. Beyond their role in solubilizing lipids, bile acids act as signaling molecules that modulate metabolic pathways and inflammatory responses within hepatocytes. Among the genes that have gained prominence in the context of NAFLD and NASH is CD163. CD163 is a surface receptor predominantly expressed on macrophages and is essential for modulating inflammatory responses. Research suggests that altered CD163 expression and function may contribute to the progression and severity of NAFLD and NASH, impacting the intricate interplay between hepatocytes, immune cells, and bile acids within the liver. Hence, this research project aims to comprehensively investigate the intricate relationship between bile acids, CD163 gene expression, and the development of NAFLD and NASH. By unraveling the underlying molecular mechanisms, this study intends to identify potential therapeutic targets and strategies for the prevention and treatment of these liver diseases, thereby alleviating their burden on global health.



Methods

To investigate the upregulation of CD163 in NASH compared to overweight individuals, we performed an analysis using the GEO2R tool and publicly available gene expression data from previous studies obtained through PubMed. Initially, a comprehensive search was conducted in the PubMed database using appropriate keywords such as "CD163," "NASH," "non-alcoholic fatty liver disease," and "Normal weight." The search aimed to identify studies that examined CD163 expression levels in NASH and the control Normal weight individuals. Selected studies were included based on predetermined inclusion criteria. These criteria included studies involving human subjects, a comparison of CD163 expression levels between NASH and Normal weight groups, and the availability of complete gene expression datasets in a GEO-compliant format. Following the selection process, we obtained the relevant gene expression datasets from the Gene Expression Omnibus (GEO) database. The datasets were processed and analyzed using GEO2R, a web-based tool specifically designed for the analysis of GEO datasets. GEO2R performs statistical analysis on gene expression data, including identifying differentially expressed genes. The CD163 expression levels in NASH and Normal weight groups were compared using appropriate statistical tests provided by the GEO2R tool. The results obtained from GEO2R were analyzed to assess the upregulation of CD163 in NASH compared to Normal weight individuals.

Results

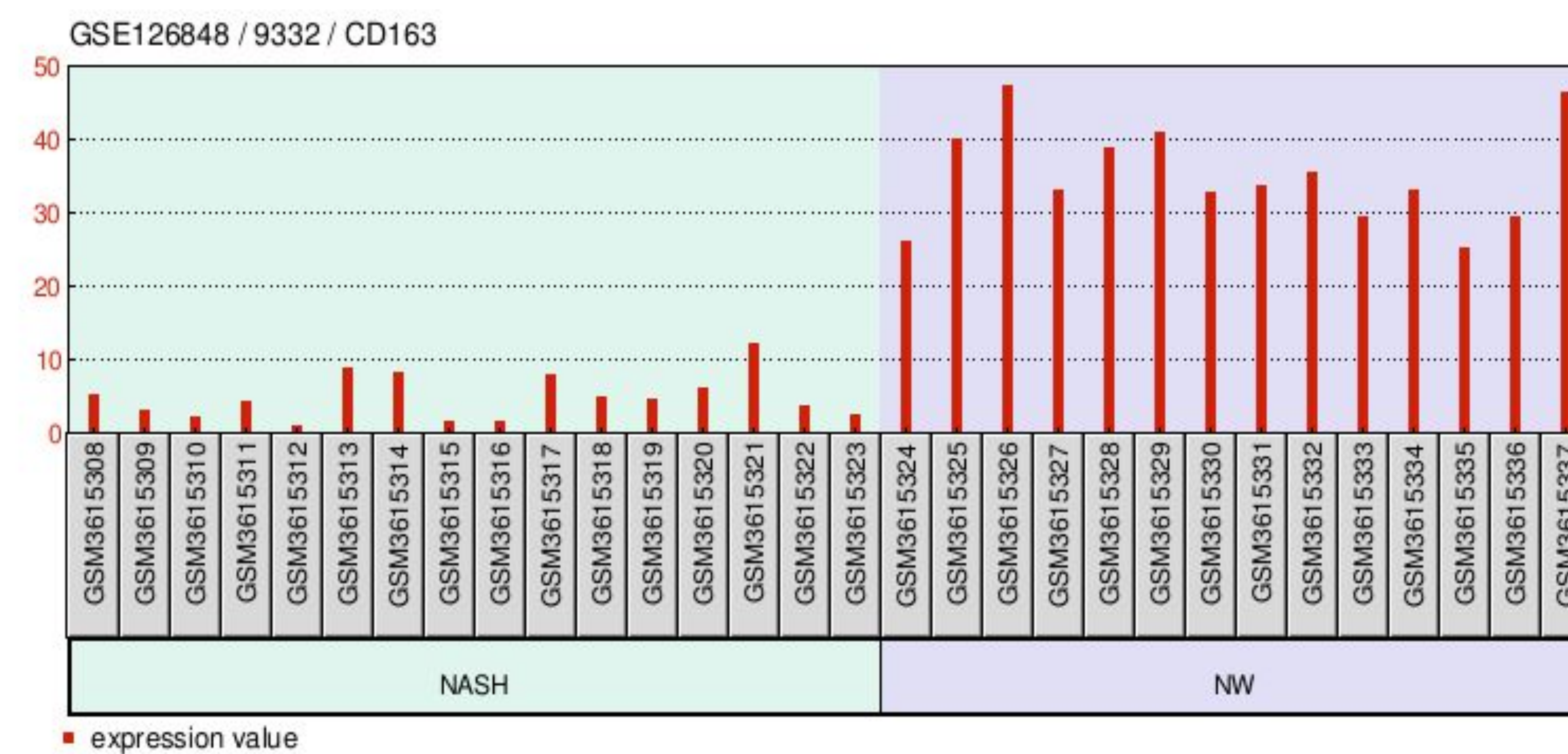
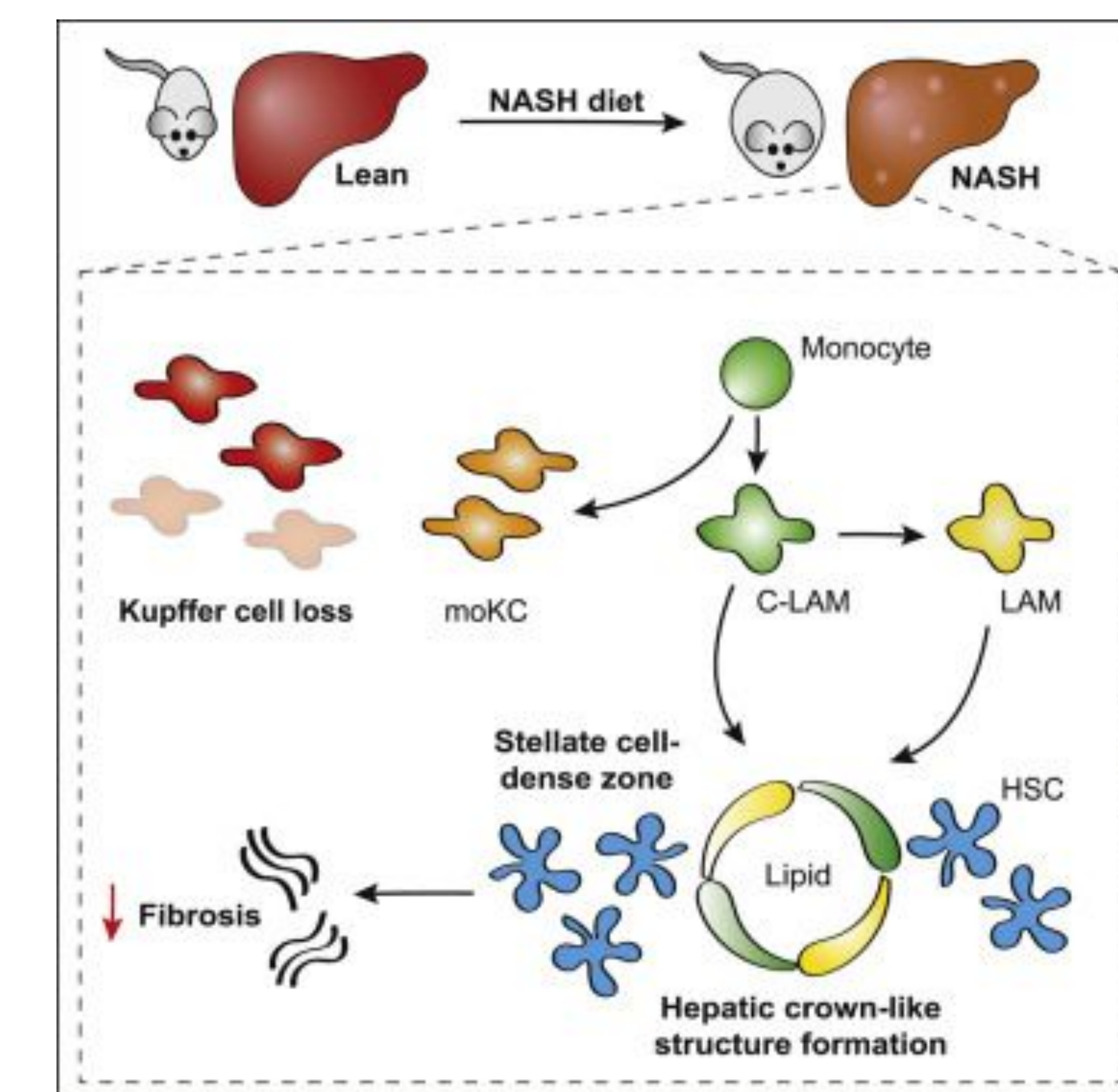


Figure 1: Displays two groups; NASH and Normal Weight and the bar graph also shows the regulation that Gene CD163 has on both groups. In this case NW has an upregulation of CD163 and is downregulated in NASH.

Discussion

The findings of this study demonstrate a significant upregulation of CD163 in normal weight individuals compared to those with Non-Alcoholic Steatohepatitis (NASH). This unexpected result may be attributed to the loss of Kupffer cells in NASH, which are known to play a crucial role in regulating CD163 expression. Kupffer cells, the resident macrophages of the liver, have been shown to express CD163 and are responsible for its clearance and regulation. CD163 is primarily expressed on macrophages and is involved in modulating inflammatory responses and scavenging hemoglobin-haptoglobin complexes. In healthy liver tissue, Kupffer cells maintain a balance in CD163 expression, keeping it at physiological levels. However, in NASH, the inflammatory microenvironment and chronic hepatocellular injury disrupt the homeostatic regulation of CD163. Studies have reported a decrease in the number and functionality of Kupffer cells in NASH, resulting in an imbalance of CD163 expression. This dysregulation may lead to the observed downregulation or lower expression of CD163 in NASH individuals compared to normal weight individuals.

Conclusion



- Further research is needed to understand why Kupffer cells are lost in NASH and how this affects CD163 expression. Additionally, it would be valuable to investigate the functional implications of increased CD163 in normal weight individuals and how it may influence inflammation in NASH.
- In summary, our study highlights the unexpected finding of increased CD163 in normal weight individuals compared to those with NASH. This difference may be due to the loss of Kupffer cells in NASH, indicating a complex relationship between CD163 levels, Kupffer cell function, and the development of NASH. These findings contribute to our understanding of CD163 regulation and suggest avenues for further research in NASH.

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