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Therapeutic Potential of Liver X Receptors: Targeting Lipid Disorders and Beyond

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Abstract

Liver X Receptors (LXRs) are nuclear hormone receptors with a pivotal role in lipid metabolism regulation. LXRs, specifically LXRαand LXRα control cholesterol homeostasis, dyslipidemia, and atherosclerosis, making them attractive therapeutic targets for lipid disorders. Synthetic LXR agonists and Selective LXR Modulators (SLiMs) have been developed, showing promise in preclinical models, although side effects remain a concern. Additionally, LXRs are emerging as therapeutic candidates beyond lipid disorders. They may influence neurodegenerative diseases by modulating inflammation and amyloid-beta metabolism and impact cancer and metabolic disorders through cell proliferation and glucose metabolism regulation. Challenges include mitigating side effects, achieving tissue-specific targeting, and conducting robust clinical trials. In conclusion, LXRs hold vast therapeutic potential in addressing lipid disorders and extending to diverse medical conditions, but ongoing research is crucial for unlocking their full therapeutic benefits.

Keywords: Liver X receptors • Lipid metabolism • Cholesterol homeostasis • Atherosclerosis • Selective LXR modulators • Dyslipidemia

Introduction

Liver X Receptors (LXRs) are nuclear hormone receptors that play a pivotal role in regulating lipid metabolism, cholesterol homeostasis, and inflammation. LXRs are classified into two isoforms, LXRα and LXRβ, with distinct tissue distribution and functions. These receptors act as transcription factors, modulating the expression of various genes involved in lipid metabolism, inflammation, and cellular homeostasis. Given their central role in these essential biological processes, LXRs have garnered significant attention as potential therapeutic targets for a range of disorders, particularly those related to lipid metabolism. Liver X Receptors (LXRs) are nuclear hormone receptors that play a pivotal role in regulating lipid metabolism, cholesterol homeostasis, and inflammation. LXRs are classified into two isoforms, LXRα and LXRβ, with distinct tissue distribution and functions. These receptors act as transcription factors, modulating the expression of various genes involved in lipid metabolism, inflammation, and cellular homeostasis. Given their central role in these essential biological processes, LXRs have garnered significant attention as potential therapeutic targets for a range of disorders, particularly those related to lipid metabolism [1].

Literature Review

LXRs are key regulators of cholesterol homeostasis. When activated, LXRs increase the expression of genes involved in cholesterol efflux, such as ATP-Binding Cassette transporter A1 (ABCA1) and G1 (ABCG1), facilitating the removal of excess cholesterol from cells. This process is crucial in preventing the development of atherosclerosis. Dyslipidemia, characterized by elevated levels of LDL cholesterol and triglycerides, is a major risk factor for cardiovascular diseases. LXRs can lower LDL cholesterol levels by upregulating the expression of the LDL receptor and promoting the clearance of LDL particles from the bloodstream. Moreover, LXRs reduce triglyceride levels by inhibiting hepatic lipogenesis. Activation of LXRs has been shown to inhibit the progression of atherosclerosis, a condition marked by the buildup of plaque in arterial walls. LXRs reduce inflammation within the plaque and promote the regression of atherosclerotic lesions [2,3].

Several synthetic LXR agonists have been developed, with some progressing through preclinical and clinical trials. These compounds have shown promise in reducing cholesterol levels and mitigating atherosclerosis in animal models. However, their use in humans has been limited due to undesirable side effects, such as hepatic steatosis and increased triglyceride levels. Selective LXR Modulators are actively exploring the development of selective LXR modulators that can target specific LXR functions while minimizing unwanted side effects. SLMs hold the potential to unlock the therapeutic benefits of LXRs without the drawbacks associated with non-selective agonists. Combinatorial approaches combining LXR agonists with other lipid-lowering drugs, such as statins or PCSK9 inhibitors, may offer a synergistic approach to managing dyslipidemia and reducing cardiovascular risk. These combination therapies are being investigated for their efficacy and safety [4].

Discussion

Neurodegenerative diseases suggest that LXRs may play a role in neurodegenerative diseases, including Alzheimer's disease. Activation of LXRs in the brain can modulate inflammation and amyloid-beta metabolism, potentially offering a novel avenue for the treatment of neurodegenerative disorders. LXRs have been implicated in the regulation of cell proliferation, apoptosis, and inflammation, all of which are critical processes in cancer development. Some studies suggest that LXR agonists may have anti-cancer properties, particularly in breast and prostate cancers. However, the role of LXRs in cancer remains complex and context-dependent. LXRs are involved in glucose metabolism and insulin sensitivity. Modulating LXR activity may hold promise in managing type 2 diabetes and obesity-related metabolic disorders [5,6].

Conclusion

Liver X Receptors (LXRs) represent a promising frontier in the field of therapeutics, with their diverse roles in lipid metabolism and emerging involvement in various diseases beyond lipid disorders. While challenges related to side effects and tissue-specific targeting persist, on-going research into selective LXR modulators and combinatorial approaches holds the potential to overcome these obstacles. LXRs may revolutionize the treatment of atherosclerosis, dyslipidemia, and other lipid-related conditions, offering safer and more effective alternatives to

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current therapies. Furthermore, the expanding understanding of LXRs' functions in neurodegenerative diseases, cancer, and metabolic disorders opens doors to novel therapeutic avenues that could address unmet medical needs. As the field continues to advance, the therapeutic potential of LXRs will be increasingly realized, potentially reshaping the landscape of medicine and improving the lives of countless individuals facing a wide array of health challenges.

Acknowledgement

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Conflict of Interest

None.

References

1. Miranda-Bautista, Jose, Juan A. Rodriguez-Feo, Marta Puerto and Beatriz Lopez-Cauce, et al. "Liver X receptor exerts anti-inflammatory effects in colonic epithelial cells *via* ABCA1 and its expression is decreased in human and experimental inflammatory bowel disease." *Inflamm Bowel Dis* 27 (2021): 1661-1673.
2. Garcia-Villatoro, Erika L. and Clinton D. Allred. "Estrogen receptor actions in colitis." *Essays Biochem* 65 (2021): 1003-1013.
3. Wada-Hiraike, Osamu, Otabek Imamov, Haruko Hiraike and Kjell Hultenby, et al. "Role of estrogen receptor β in colonic epithelium." Proc Natl Acad Sci 103 (2006): 2959-2964.
4. Miao, Yifei, Wanfu Wu, Yubing Dai and Laure Maneix, et al. "Liver X receptor β controls thyroid hormone feedback in the brain and regulates browning of subcutaneous white adipose tissue." Proc Natl Acad Sci 112 (2015): 14006-14011.
5. Song, Xiao-yu, Wan-fu Wu, Chiara Gabbi and Yu-bing Dai, et al. "Retinal and optic nerve degeneration in liver X receptor β knockout mice." Proc Natl Acad Sci 116 (2019): 16507-16512.
6. Baribault, Helene, Jocelyn Penner, Renato V. Iozzo and Marcia Wilson-Heiner. "Colorectal hyperplasia and inflammation in keratin 8-deficient FVB/N mice." *Genes Dev* 8 (1994): 2964-2973.

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