

Diverse Molecular Mechanisms in Liver Cell Proliferation

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Introduction

Researchers found that microRNA-126a, specifically originating from liver sinusoidal endothelial cells, is critically involved in supporting and fostering hepatocyte proliferation. This action is achieved through its precise targeting of PIK3R2, a protein deeply involved in various aspects of cell signaling, consequently facilitating and promoting comprehensive liver regeneration by boosting cell division.[1]

The absence of FOXO1 in liver cells markedly boosts their growth and exhibits a clear propensity to contribute to tumor development. The underlying mechanism for this effect is that the loss of FOXO1 results in an elevated activity level of YAP/TAZ, which are key proteins that actively drive cell division and expansion, thereby deregulating normal cellular control.[2]

MicroRNA-203a-3p functions as a significant inhibitor of liver cell growth and actively promotes their programmed cell death, known as apoptosis. This suppressive action is accomplished by specifically targeting FOXM1, a protein well-known for its role in promoting cell division, thereby meticulously regulating the delicate balance of liver cell populations within the tissue and preventing excessive growth.[3]

SALL4 stands out as a pivotal protein that directly and potently stimulates the proliferation of liver cells. Its mechanism involves the direct transcriptional activation of the IGF2 gene, which is widely recognized for its critical role in promoting cell proliferation, consequently playing an instrumental role in the crucial process of liver regeneration and tissue repair.[4]

Circular RNA circRNA_0000720 functions as a potent molecular promoter for hepatic cell growth. This is accomplished by acting as a "sponge" for miR-101-3p, preventing this microRNA from inhibiting certain target genes, which in turn leads to the subsequent activation of the Wnt/ β -Catenin signaling pathway, a pathway well-established as a key driver of cell proliferation and development.[5]

KIF20A is recognized for its substantial contribution to fostering both the growth and migratory capabilities of liver cells. This influence is exerted by modulating the activity of the AKT signaling pathway, a critical route for ensuring cell survival and robust proliferation, thus significantly contributing to the vital processes involved in liver regeneration and tissue remodeling after injury.[6]

The long non-coding RNA HNF1A-AS1 is absolutely essential and instrumental in facilitating liver cell proliferation. Its mechanism of action involves the intricate regulation of miR-140-5p, an important microRNA, consequently exerting its influence over the complex molecular pathways that are crucial for driving cellular division and overall liver regeneration and repair processes.[7]

SIRT6 actively enhances the growth of liver cells and provides robust protection

against programmed cell death, known as apoptosis, particularly within the context of hepatocellular carcinoma that is linked to Non-Alcoholic Fatty Liver Disease. This dual protective and proliferative effect is achieved by its crucial role in activating the AKT signaling pathway, a well-known modulator of cell survival and growth.[8]

The long non-coding RNA H19 actively stimulates liver cell proliferation through its intricate influence on the miR-19b-3p/SIRT1 axis. This complex interaction is vital for regulating key cellular pathways, which ultimately culminates in the promotion of hepatocyte growth and tissue regeneration, underscoring its importance in maintaining liver homeostasis.[9]

Exosomes, tiny vesicles carrying miRNA-125b, released specifically by liver sinusoidal endothelial cells, are recognized for their vital and encouraging role in promoting liver cell growth after partial hepatectomy. This particular mechanism is absolutely crucial for underpinning the liver's remarkable regenerative capacity following various forms of injury or surgical intervention, aiding in recovery.[10]

Description

Researchers found that microRNA-126a, specifically originating from liver sinusoidal endothelial cells, is critically involved in supporting and fostering hepatocyte proliferation. This action is achieved through its precise targeting of PIK3R2, a protein deeply involved in various aspects of cell signaling, consequently facilitating and promoting comprehensive liver regeneration by boosting cell division [1]. The absence of FOXO1 in liver cells markedly boosts their growth and exhibits a clear propensity to contribute to tumor development. The underlying mechanism for this effect is that the loss of FOXO1 results in an elevated activity level of YAP/TAZ, which are key proteins that actively drive cell division and expansion, thereby deregulating normal cellular control [2]. MicroRNA-203a-3p functions as a significant inhibitor of liver cell growth and actively promotes their programmed cell death, known as apoptosis. This suppressive action is accomplished by specifically targeting FOXM1, a protein well-known for its role in promoting cell division, thereby meticulously regulating the delicate balance of liver cell populations within the tissue and preventing excessive growth [3].

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SIRT6 actively enhances the growth of liver cells and provides robust protection against programmed cell death, known as apoptosis, particularly within the context of hepatocellular carcinoma that is linked to Non-Alcoholic Fatty Liver Disease. This dual protective and proliferative effect is achieved by its crucial role in activating the AKT signaling pathway, a well-known modulator of cell survival and growth [8]. The long non-coding RNA H19 actively stimulates liver cell proliferation through its intricate influence on the miR-19b-3p/SIRT1 axis. This complex interaction is vital for regulating key cellular pathways, which ultimately culminates in the promotion of hepatocyte growth and tissue regeneration, underscoring its importance in maintaining liver homeostasis [9].

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Conclusion

Recent investigations into liver cell proliferation reveal a complex network of molecular regulators. MicroRNA-126a, originating from liver sinusoidal endothelial cells, plays a crucial role by targeting PIK3R2 to promote liver regeneration [1]. In contrast, the absence of FOXO1 in hepatocytes significantly encourages growth and can contribute to tumor development, primarily through YAP/TAZ activation [2]. MicroRNA-203a-3p offers a counter-regulatory mechanism, suppressing hepatocyte proliferation and promoting apoptosis by targeting FOXM1 [3]. Further studies identify SALL4 as a direct stimulant of liver cell growth, achieving this by activating the IGF2 gene [4]. Circular RNA circRNA_0000720 also promotes growth by "sponging" miR-101-3p and activating the Wnt/ β -Catenin pathway [5]. KIF20A is crucial for encouraging both growth and migration of liver cells, influencing the AKT signaling pathway [6]. Similarly, the long non-coding RNA HNF1A-AS1 promotes proliferation by regulating miR-140-5p [7]. SIRT6 enhances liver cell growth and protects against programmed cell death, particularly in the context of Non-Alcoholic Fatty Liver Disease-associated hepatocellular carcinoma, via AKT pathway activation [8]. Another long non-coding RNA, H19, stimulates proliferation through the miR-19b-3p/SIRT1 axis [9]. Finally, exosomes carrying miRNA-125b, released by liver sinusoidal endothelial cells, are vital for encouraging liver cell growth after partial hepatectomy, underscoring their role in regenerative capacity [10]. These

findings collectively highlight diverse molecular mechanisms governing liver cell growth and regeneration.

Acknowledgement

None.

Conflict of Interest

None.

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