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The pivotal role of IL-17A in hepatic stellate cell activation

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Biliary atresia (BA) is a devastating neonatal cholangiopathy marked characterized by progressive bile duct obstruction, leading to liver fibrosis and ultimately cirrhosis [1]. Despite advances in surgical interventions, the challenge of managing progressive hepatic fibrosis persists. The recent study by Jiang *et al*. entitled "IL-17A promotes glycolysis to activate human hepatic stellate cells by mediating the TRAF2/TRAF5/HUR/PFKFB3 axis" sheds light on a novel metabolic mechanism driving liver fibrosis in BA.

The authors meticulously demonstrate that interleukin 17A (IL-17A), a pro-inflammatory cytokine, is significantly upregulated in liver tissues of BA patients. Their findings elucidate a mechanistic pathway in which IL-17A facilitates hepatic stellate cell (HSC) activation and fibrosis through enhanced glycolysis. Central to this process is the formation of a TRAF2/TRAF5/HUR complex that stabilizes PFKFB3 mRNA, thereby boosting glycolytic activity [2].

Glycolysis, often associated with tumor metabolism, emerges here as a critical driver of HSC activation. Elevated PFKFB3, a key glycolytic enzyme, underscores the metabolic reprogramming necessary for fibrogenesis [3, 4]. The study's use of glycolytic inhibitors such as 2-deoxy-D-glucose (2-DG) effectively attenuated IL-17A-induced HSC proliferation and fibrosis, highlighting the therapeutic potential of targeting metabolic pathways in BA.

Moreover, exploring the TRAF2/TRAF5/HUR axis advances our understanding of cytokine-mediated post-transcriptional regulation in liver fibrosis. The interplay between immune signaling and metabolic reprogramming represents a paradigm shift in how we perceive fibrotic diseases, offering new therapeutic avenues.

Complementing this perspective, a study previously reported in CEJI, by Liang Miao *et al*. (2023), evaluated the efficacy of direct antiviral drugs in improving liver fibrosis in chronic hepatitis B patients. Their findings emphasize the importance of metabolic and immune modulation in managing liver fibrosis, reinforcing the notion that targeted therapies addressing both viral load and fibrogenic pathways can yield significant clinical benefits [5].

The present study is timely, aligning with the growing interest in immunometabolism [6-8]. Targeting IL-17A or its downstream metabolic pathways could pave the way for adjunctive therapies aimed at halting or reversing hepatic fibrosis in BA, complementing existing surgical approaches.

We invite you to read this interesting paper.

Piśmiennictwo

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