An article published recently in Cancer Research elegantly performed lipidomic and gene expression analyses in a murine model of nonalcoholic steatohepatitis (NASH)–associated hepatocellular carcinoma (HCC) and compared the findings with serum samples from patients with fibrosis and HCC (1).

The study reports that the expression of the C18 fatty acid producing elongase (ELOVL6) is elevated in a mouse NASH model. The animals also exhibited elevated oleic acid (18:1n9) and vaccenic acid (18:1n7) abundance in livers and serum. Thereby, the study supports findings about increased hepatic ELOVL6 expression in other models of NASH, such as a fructose feeding model (2) and low-density lipoprotein receptor (LDLR) knockout animals fed on a Western-type diet (3). In line with these findings, a causal role for ELOVL6 in the development of NASH was published recently in a comprehensive work using overexpression and knockdown strategies (4).

HCC represents a rare but important complication of NASH (5). The study by Muir and colleagues reports an increased expression of ELOVL6 not only in murine NASH but also in murine NASH–associated HCC. Because lipidomic analyses of sera of 15 patients with HCC showed a higher prevalence of the C18 vaccenic acid (18:1n7) than serum of patients with cirrhosis, the authors suggested elevated ELOVL6 expression in human HCC. Although they observed lower levels of the more abundant linoleic acid (18:2n6) and they do not show any data on ELOVL6 expression in patients with HCC, they propose ELOVL6 as a pharmacologic target for patients predisposed to HCC.

We investigated differential ELOVL6 gene expression between HCC (n = 247) and nontumor (n = 239) samples of a Gene Expression Omnibus dataset (GSE14520; see Fig. 1). Interestingly, in contrast to Muir and colleagues, our results from this large dataset revealed significantly decreased levels of ELOVL6 gene expression in the majority of human liver tumors compared with nontumorous tissue. We also observed a decreased expression of Elovl6 in the widely accepted murine diethylnitrosamine (DEN) HCC model (see Fig. 2; ref. 5).

Taken together, different recent reports from the literature suggest a pathophysiologic role for ELOVL6 in steatohepatitis. Still, a role for ELOVL6 in HCC is as yet elusive and our data show ELOVL6 expression to be reduced in a common murine non-NASH–associated HCC model as well as in a large proportion of patients with HCC. In our opinion, the data available on ELOVL6 in HCC do not justify proposing ELOVL6 as a therapeutic target in either prevention or treatment of HCC.
Disclosure of Potential Conflicts of Interest
No potential conflicts of interest were disclosed.

References
Lipid Metabolism Signatures in NASH-Associated HCC—Letter
Sonja M. Kessler, Stephan Laggai, Ahmad Barghash, et al.

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