論 文 審 査 の 結 果 の 要 旨

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（論文審査の結果の要旨）

Trans-fatty acids (TFA), unsaturated fatty acids (FA) containing *trans* double bonds, are reported to be more harmful to humans compared with other FA. Peroxisome proliferator-activated receptor α (PPARα) is a ligand-activated nuclear receptor that regulates lipid homeostasis, inflammation, and immune responses, but the role of PPARα in TFA-induced liver abnormalities remains unclear.
To examine the contribution of PPARα to changes in liver phenotypes induced by TFA, two diets were used: a purified control diet and an isocaloric diet where most of the FA are replaced with TFA. The diets were fed to wild-type and *Ppara*-null mice for two months and liver phenotypes were examined.

その結果、「胡暁」は以下の結論を得た。

1. TFA-containing diet-fed *Ppara*-null mice developed more severe hepatic steatosis and inflammation compared with the similarly-treated wild-type mice.
2. The TFA-containing diet increased hepatic expression of enzymes involved in *de novo* FA synthesis and decreased TG-hydrolyzing enzymes in both genotypes, but the expression of FA-catabolizing enzymes were decreased in *Ppara*-null mice only.
3. More severe hepatitis observed in TFA-containing diet-treated *Ppara*-null mice was likely derived from increased toll-like receptor 2 expression and ensuing nuclear factor-kappa B activation.

The present results showed one of the mechanisms of steatogenesis caused by excessive TFA consumption and a protective role of PPARα for TFA-induced liver abnormalities. Since hepatic expression of PPARα is documented to be significantly reduced with fibrosis progression in the patients having non-alcoholic steatohepatitis, restriction of TFA intake might be useful for such patients. Additionally, therapeutic interventions to maintain PPARα function might be beneficial to reduce TFA-induced hepatotoxicity.

これらの結果は、非アルコール性脂肪性肝炎の発症における食事中トランス脂肪酸や核内受容体 PPARα の関与を理解するうえで、重要な知見であると考えられた。従って主査、副査は一致して本論文を学位論文として価値があるものと認めた。