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A low fish oil inhibits SREBP-1 proteolytic cascade, while a high-fish-oil feeding decreases SREBP-1 mRNA in mice liver: relationship to anti-obesity.

Nakatani T, Kim HJ (金 賢珠) , Kaburagi Y, Yasuda K, Ezaki O

Division of Clinical Nutrition, National Institute of Health and Nutrition, 1-23-1 Toyama, Shinjyuku-ku, Tokyo 162-8636, Japan.

Rodents fed fish oil showed less obesity with a reduction of triglyceride synthesis in liver, relative to other dietary oils, along with a decrease of mature form of sterol regulatory element binding protein-1 (SREBP-1) and activation of peroxisome proliferator-activated receptor alpha (PPAR α). Decrease of mature SREBP-1 protein by fish oil feeding was due to either inhibition of SREBP-1 proteolytic cascade or to decrease of its mRNA. To clarify its mechanism and relation to antiobesity effect, mice were fed fish oil in a range from 10 to 60 energy percent (en%). Fish oil feeding decreased body weight and fat mass in a dose-dependent manner, in parallel with PPAR α activation and a decrease of SREBP-1 mRNA. However, compared with 0 en% fish oil feeding, 10 en% fish oil feeding decreased mature SREBP-1 protein by 50% with concomitant decrease of lipogenic genes, while precursor SREBP-1 protein rather increased by 1.3-fold. These data suggest that physiological doses of fish oil feeding effectively decrease expression of liver lipogenic enzymes by inhibiting SREBP-1 proteolytic cascade, while substantial decrease of SREBP-1 expression is observed in its pharmacological doses, and that activation of PPAR α rather than SREBP-1 decrease might be related to the antiobesity effect of fish oil feeding.